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WILLIAM CRAWFORD GORGAS ISSUE

August. 1950

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GUEST EDITORIAL

Health Legislation

1950

IN these fast-moving, modern times, it is almost an axiom that no state can continue to prosper in health or wealth without benefit of a well-balanced, progressive public health program.

Such a program is brought into being by the demands of the citizens as expressed through their elective representatives. Without laws, for example, a modern sanitation program would fall before the positive forces of avarice and the negative rot of laxity and indifference. Without appropriations, operating costs of life-preserving services could not be met.

The Virginia General Assembly in 1950 studied the various phases of the public health program and found some worthy of expanded service and others in need of greater legal support. As a result of legislation by this body, industrial health, venereal disease control, cancer control and other programs were further improved and increased in effectiveness and value.

Bills sponsored by the State Health Department were few in number, but all were enacted into law, and each undoubtedly will have an important part in the improved health picture of the Commonwealth.

The following health laws will become effective July 1, 1950. Although not all were sponsored by the State Health Department, each of them is part of the general public health program and receives the hearty support of state health workers.

CANCER REPORTING LEGALIZED. The General Assembly made it legal for hospitals to give statistical information to the State Health Department for use in cancer research. According to the law, each hospital and clinic within the state may make available to the cancer bureau abstracts of their records on patients having malignant tumors and cancers.

Actually the Health Department has been briefing records for some time in many hospitals. The legality of the procedure has been questioned, however, and certain hospitals have been reluctant to part with the desired data.

This information is recorded in a central registry. Included are final facts concerning the prevalence of cancer in the state, the geographic distribution of cases; the anatomical location of cancers; the division of victims by age, sex, and color; survival periods; and life expectancy. The information is confidential and published only in the form of statistics without identification of individual cases.

INDUSTRIAL HEALTH BILL. The State Health Department was authorized by law to survey health hazards in industrial plants.

In the past, personnel of the Bureau of Industrial Hygiene have worked in this connection only when requested. Many industries have welcomed the service, but a small fraction of the plant operators have been hostile, refusing entrance to engineers to survey their plants. The new law will do much to alleviate this unfortunate situation.

Each year thousands of dollars are paid out by industries as compensation to workers with occupational disease claims which come within the provisions of the Virginia Workmen's Compensation Act. No legal steps have been taken previously to prevent these cases before they occurred. Under provisions of the new law it will be possible to apprize operators of hazards within their plants, possibly preventing many of these diseases and accidents for which claims are made.

The Bureau of Industrial Hygiene is staffed with experienced personnel and has specialized equipment that would be uneconomical for small private industries to own. Whether the operators of the plants surveyed will heed the recommendations of these engineers and take steps to protect workers, remains to be seen. It is believed, however, that this legislation will go a long ways toward preventing occupational diseases.

PRENATAL SEROLOGICAL EXAMINATION. This law requires that a blood test be made of each pregnant woman to determine whether or not she has syphilis.

Syphilis is the cause of death in 80% of the children born of infected mothers. To live without treatment is a worse tragedy than early death for these children. If syphilis is detected, however, treatment is rapid and beneficial as late as the fifth month of pregnancy.

All positive syphilis tests must be filed with the Bureau of Venereal Disease Control. There the information will be kept confidential and not published except in statistical form without identification of person.

DENTAL HYGIENISTS LICENSED. Legislation was enacted, defining dental hygienists and licensing their practice. A dental hygienist is a person trained in the practice of cleaning and polishing teeth. According to the Act, their function is to assist members of the dental profession in providing oral health care to the public.

The hygienist is to work under the direction of a registered dentist of this state. She may remove calcareous deposits and stains, polish, and make topical applications of medicinal agents to the teeth for prophylactic purposes.

Dental hygienists will be used in the dental program of the Health Department.

CONFIDENTIAL NATURE OF VITAL RECORDS ENDORSED. A law was passed providing that a full birth certificate shall be issued only upon the discretion of the State Registrar, except when sought by the person registered if he is of age, by his legal representative, or by court order. This will protect confidential information about births,

Death records are also protected, the bill providing that certified copies of a death record may be issued only to a legal representative of the deceased or to a person having a direct interest in the matter recorded, or by court order. Records that are confidential encourage more accurate and complete registration and help eliminate needless embarrassment to illegitimate children or their parents.

The importance and need to the individual as well as to Public Health programs of Vital Records is continually increasing. This new law is believed to be a step toward safeguarding and protecting these records in the interest of both.

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MEDICAL SCHOLARSHIPS PROVIDED. The General Assembly authorized the University of Virginia and the Medical College of Virginia to establish annually 20 medical scholarships each and Virginia State College to establish 10 annual scholarships to Virginia students attending Meharry Medical College, Nashville, Tennessee.

Before any scholarship is awarded, the applicant must sign a written contract that includes, among other things, a stipulation that he engage in the general practice of medicine in a rural community in Virginia. Selection of the community will be his own, but his selection will be from one approved by the State Health Commissioner. Under the terms of the contract the applicant must agree to practice for a period of years equal in number to the years that he was beneficiary of his scholarship.

Six annual nursing scholarships for each congressional district were established by the Legislature. Twenty nursing scholarships for Negroes were established to be awarded from the state at large. These scholarships will be made by the State Board of Health.

Many rural Virginia counties desperately need more active doctors and nurses. The financial aid provided by these scholarships may encourage more students to engage in rural practice, thereby relieving the general scarcity of medical people in those areas.

L. J. ROPER, M.D.,
State Health Commissioner of Virginia.

Floral Eponym

Caralluma Dalzielli

DALZIEL, JOHN MCEWEN, 1872-1948

DALZIEL was born at Nagpur, India on May 16, 1872 and died at Chiswick (London), February 21, 1948. He was educated at Dollar Academy, Scotland, and at Edinburgh University, where he studied medicine and took the degree of M.B. (later qualifying as M.D.). Upon leaving the University he spent some six years in South China as a Presbyterian medical missionary. In 1902 he joined the West African Medical Service and served in Northern Nigeria and later at Accra on the Gold Coast. Upon his retirement, in 1923, he worked at Kew Herbarium, collaborating with Dr. J. Hutchison in writing "Flora of West Tropical Africa". He added an appendix to this work, "Useful Plants of West Tropical Africa" (1937), recording the medical usage of these plants. This is now an authoritative work. Previously, (1916) he wrote "A Hausa Botanical Vocabulary". He also collected insects of importance as vectors in tropical medicine and presented his collection to the University of Edinburgh.

Caralluma dalzielli is a species of the milk weed family.

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MANAGEMENT OF DELIRIUM IN THE GENERAL HOSPITAL*

PATRICK H. DREWRY, JR., M.D.,†
and
JAMES B. FUNKHOUSER, M.D.,†
Richmond, Virginia.

The word "delirium" originally was used to denote any type of mental illness, but in the course of time has come to have a more circumscribed meaning. It is now regarded as a disorder of the sensorium in which orientation is impaired, the critical faculties are blunted or lost, and thought content is irrelevant and incoherent. Commonly there are illusions or hallucinations, and frequently there is a marked fear reaction. The degree of delirium may vary from a mild state of mental confusion which is brief in duration to an acute and severe reaction in which the patient is almost uncontrollable. It occurs typically as a result of either endogenous or exogenous toxic processes. The endogenous processes are exemplified by infection, metabolic disturbances, anoxia or the retention of waste products. The exogenous toxic processes are brought about by the introduction of some drug such as the barbiturates or alcohol. Frequently there is a combination of both endogenous and exogenous factors, and thus we find that due to disturbed metabolism some otherwise safe and harmless sedative adds to the delirium, due to faulty or incomplete elimination by a diseased or damaged excretory function.

Although there has apparently been some decrease statistically in the incidence of fatal delirium within the past decade, the reaction is still a relatively frequent one and is a problem which as a rule must be handled in a general medical or surgical hospital. A delirious patient in such a hospital usually presents an acute problem and is often an administrative, if not a medical, emergency. It is felt that the situation is frequently misunderstood and managed in an unsatisfactory way, thus leading to embarrassment for the doctor, anxiety for the nurses, and danger for the patient. It is also believed that most mistakes are due to failure to recognize the condition in its early stages with a resulting delay in the institution of proper therapeutic and preventive measures. It is the purpose of this paper to discuss the early signs of delirium and to suggest a method of management. It is to be understood, of course, that the first procedure is to treat the disease which is producing the delirium, but in this paper, discussion will be limited to the management of that symptom-complex alone.

Delirium is a disease of the night, and it is believed that this is the chief reason for failure to recognize its existence early, for examination of the records of delirious patients shows in many cases that the patients had been mildly delirious for several days prior to the time the physician became aware of it. *During the daylight hours, particularly the morning hours, the patient may be mentally clear.* At the end of the day the physical factor of exhaustion and the psychological factors of light and shadow combine to make the evening and night critical times. A mildly delirious patient or one who is in a pre-delirious stage may exhibit only slight restlessness, apprehension, inattention, and a tendency to give irrelevant or incoherent replies to questions. The only significant complaints of the patient may be of insomnia or bad dreams, and such symptomatology is easily overlooked when morning rounds are made because the patients are apt to minimize, rationalize or deny that such symptoms have been present during the night. Not infrequently a patient who has had hallucinations during the night will state in the morning, if asked, that he remembers having had a few bad dreams during the night, but that otherwise he rested comfortably. The night nurse is not present to give her account of the patient's talk and behavior during the night, and in her report she may merely have described his behavior as "restless". Even if she has written a detailed statement of his mental symptoms, the physician may not have read the note.

Another reason for failing to recognize the existence of delirium in its early stages is that the physician is preoccupied with the medical or surgical condition in which he is primarily interested. For example, the physician who is treating a patient with cardiac decompensation is primarily interested in restoring compensation and perhaps does not even think of the possibility of delirium. Yet, in a series

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*Read before the annual meeting of the Medical Society of Virginia at Fort Monroe, October 9-12, 1949.

of cases studied by one of us in a general hospital it was found that 8% of patients admitted for cardiac disease had some degree of delirium at one time or another during their hospitalization. The following case illustrates the development of delirium and some of the factors which led to the failure of the physician to realize its existence in its early stages:

The patient was a 45 year old man who had used alcohol regularly for 20 years, but not to the extent of interfering with his work. He was admitted to the hospital because of a broken leg. On the first night after admission the nurse's notes showed that at 1:00 A.M. she had found him standing by the window in his cast, and had difficulty in persuading him to get back in bed. When questioned about it in the morning, the patient said he was accustomed to having plenty of air at night and that he had left his bed to try to open the window. Sodium amytal was ordered the next night to insure sound sleep. The nurse's notes for that night indicated that he was up all night, said he was expecting visitors, was not aware of what time it was, was noisy and generally uncooperative. On morning rounds, however, the patient was found to be oriented and cheerful, almost to the point of gaiety, although slightly excited and with a moderate elevation of temperature. There was no evidence of any mental derangement, and the physician disregarded the nurse's note. The patient slept quietly all afternoon, but on the third night the supervisor called the physician to report that he had left the hospital in his bed clothes and four men were required to drag him back to his bed. He was in a state of panic, and was screaming that the F.B.I. was after him.

This case illustrates the fact that delirium usually has an insidious onset and that one can fail to recognize its existence due to the fact that it is at night that the first symptoms usually begin and the symptoms may show a diurnal variation.

In the management of the delirious patient there are psychological as well as physical factors to be considered. Nurses are trained to keep the sick room as quiet as possible, particularly at night. Lights are shaded, corridor conversations are held in whispers, and footsteps are on tiptoe. As darkness closes in, half-open doors, bed screens and the blowing of window curtains cast unfamiliar shadows. Unidentified, partially muffled sounds come from adjoining rooms. Furthermore, since the nurse is required to determine whether patients are sleeping well, she may tiptoe around with a shaded flashlight, peering into the patients' faces to see whether they are asleep. In a setting such as this it is easy for the partially clouded brain of an acutely ill patient to misinterpret what he sees and to develop illusions and hallucinations.

It is a well established fact that a delirious patient, especially in the early stages of delirium, can often be successfully diverted if his attention is engaged by conversation, banter, questioning, examination, etc., much as a child who wakes frightened in the night has to have his fears removed. Delirious patients are extremely suggestible, but the very suggestibility which can turn a shadow into a snake and a window curtain into a ghost may be used with good therapeutic results. The psychological aspect of the management of delirious patients should be in accord with an understanding of the facts mentioned above. The patient who is showing any evidence of developing delirium should be in a room where the lights can be turned on without disturbing others. Ideally, he should have a night nurse who can be present to reassure him at any time that he appears frightened or anxious. Patient, continuous, persuasive conversation, diversion, a well-lighted room and a matter-of-fact tone of voice may literally "bring the patient to his senses". Furthermore, of definite importance in the nursing management of such patients should be the concentration of all personnel concerned, around the clock, to readjust the patient's waking and sleeping hours so that the vicious circle of turning the night into day is broken. A rigid insistence that the patient stay awake during daytime hours often makes sleep more possible at night. Patients who are permitted to lie awake all night and sleep all day will take a more protracted course in recovering from delirium.

Prophylaxis is another factor in the management of delirious patients. The knowledge of the type of patient who is likely to develop delirium has often prevented cases from developing. Patients with acute infectious diseases, particularly where the illness is of long duration, such as typhoid fever or those in which there is an unusually high temperature, as lobar pneumonia, constitute one group. Other groups are post-operative patients, especially those who have lost an unusually large quantity of blood, physically exhausted patients such as those who have not slept for long periods of time or have become dehydrated,

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and, finally, uremic or cardiovascular patients whose brains are likely to suffer from anoxia are also prone to develop a toxic psychosis. In such cases, with endogenous factors already at work, an addition of exogenous toxins, such as alcohol or drugs, may be hazardous. The actual function of the liver as a detoxifying agent is still unfortunately obscure, but it is known that this is one of its most important functions. It is puzzling as to the exact part the various vitamins play in the toxic psychoses, but it is certain that avitaminosis is clinically very important in the production of delirium. Glucose and certain of the vitamin B group are indispensable in both the brain and the liver. The incidence of delirium is very striking in patients with damaged liver function and in our series of cases we have come to suspect that a diseased liver is present in the majority.

It follows then that in the prophylactic treatment for delirium, combating the tendency to dehydration, avitaminosis and starvation are of great importance. When the patient has been taking barbiturate sedatives these drugs should be withdrawn immediately, since barbiturates are destroyed in the liver, and if the liver function is damaged an excessive quantity of drug will accumulate in the body. Sometimes the mere withdrawal of such sedative medication is all that is necessary. However, when violence must be controlled and sleep is imperative, paraldehyde should be given since it is excreted by the lungs in large part rather than the liver. The quantity of sedative medication which is given should be that which is sufficient to produce the desired results. We find that many patients are kept in a state of excitement by quantities of sedation which are sufficient to release inhibitions but not sufficient to produce sleep. The individual who has developed, or might develop, delirium should be given an adequate quantity of sedation to induce sleep, if sedation is necessary. Paraldehyde is a safe sedative, and most adults can tolerate a dose of 4 drams or more without any adverse effect. The authors believe that a great many cases of delirium are actually drug intoxications.

In any case of delirium, since there may be liver damage or inadequate excretion of toxic products, it is felt that glucose, thiamine and vitamin B complex and as much fluid and nourishment as can be retained should also be given.

It is a recognized fact that a routine schedule of treatment for any type of illness is not satisfactory, since individuals vary in their reactions. However, it is felt that it may be of value to suggest a schedule for an average patient who is developing, or has developed, a delirious reaction. Let us consider the patient to be an adult male, whose weight is about 150 pounds. He has been admitted to a general hospital with a serious medical or surgical illness, and has begun to show the early signs of delirium mentioned previously. The suggested management of his case is as follows:

(1) The illness responsible for admission should be properly treated.

(2) The patient should be placed in a single room, preferably one which has a special type of screen which will prevent him from getting out of the window. If this type of screening is not available, he should at least be on the ground floor.

(3) The lighting of the room should be such that no puzzling or disturbing shadows are cast at night. If his condition permits, he should be kept awake during the daytime. In many cases, 5-10 mgm. of benzedrine at about 9:00 A.M. will serve the double purpose of keeping the patient awake during the early part of the day, and of producing a temporary sense of well-being.

(4) There should be a special attendant, especially at night, preferably one who is trained in the management of such cases, but, if not, an individual of reasonably good intelligence who can talk with the patient and relieve him of his fears.

(5) It is essential that the patient receive an adequate amount of food, high in carbohydrates and proteins, unless there is some definite contraindication to this. The nurse may be required to spoon-feed the patient.

(6) Liquids must be given in quantity, preferably by mouth, but intravenously if necessary.

(7) Vitamins of the "B" group are essential, and the patient should receive 150 mgm. of thiamine chloride, t.i.d., by mouth, if possible. Most patients are able to take this, and it should be supplemented by 1,000 c.c. of 5% glucose in saline with one or more ampules of vitamin B complex (such as "Solu-B") daily if necessary.

(8) Where the patient is too restless or agitated to permit the administration of such a quantity of fluid intravenously, 50 c.c. of 50% glucose, with insulin, u 20, and the vitamin B complex added, may be used.

(9) Finally, where it is essential that sedation be

given, it is suggested that paraldchyde, Z IV, be given. This may be repeated in two hours, if necessary.

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DISCUSSION

DR. SIDNEY G. PAGE, JR., Richmond: The points mentioned in this paper stress ideas in the care of patients with acute delirium which are seldom noted in text-books. Such matters as having patients sleep at night and kept awake during the day, avoiding unnecessary use of sedatives, particularly in those patients with sick livers or in those patients with very high temperatures in whom delirium is impending, as well as reassurance of frightened patients who need support of this type, are all particularly helpful points. Doctor Funkhouser has touched on the important role of impaired liver function in the causation of delirium, and suggests more liberal use of paraldehyde in place of barbiturates. It has been stated before that if a pleasant tasting and smelling paraldehyde could be devised, this very satisfactory drug would largely replace barbiturates in conditions such as acute delirium.

Prophylactic treatment for delirium such as combating dehydration, avitaminosis and starvation cannot be overemphasized and the speaker has indicated a very helpful outline for the prevention of delirium, as well as the treatment of such condition. If these points are kept in mind and used, there will be less acute delirium seen in the general hospitals.

DR. JAMES OTEY BURKE, Richmond: Doctors Drewry and Funkhouser have brought to our attention an important feature of many illnesses. As general practitioners, internists and surgeons, we have frequently considered delirium only as a necessary complication of some serious illnesses.

As they have implied, the cardiac patient may have delirium as a result of anoxia. Fever alone may be the factor in some febrile diseases. I would like to comment chiefly on the role of the liver in the production of delirium.

The mechanisms of relationship between hepatic function and brain function are not clear. Mahaim has produced diffuse ganglion cell disease in the brain by experimental liver damage.

Basal ganglion degeneration in dogs has followed common bile duct ligation.

Degenerative glial changes have been noted in acute yellow atrophy and cirrhosis.

The most striking clinical indication of relationship occurs in the hepato-lenticular degeneration of Wilson's disease. We recognize hepatic coma, but we cannot always demonstrate, in bio-chemical terms, the difference between a case of severe hepatitis without nervous system symptoms and one with nervous system symptoms. In some, hypoglycemia accounts for the difference. Thiamin and niacine help some, but not all. No difference may be noted in the fetor hepatitis of the two patients. We are sure that there is a difference between these two patients but cannot always prove it by our ordinary laboratory means.

A possible relationship between the liver and brain cell activity is suggested by a glutamic acid linkage as follows:

Nerve cell potential is intrinsically based on acetylcholine release. Nachmansohn has shown that glutamic acid may act as a coenzyme of choline acetylase in that it increases the formation of acetylcholine.

Zimmerman and others have shown glutamic acid is beneficial to intelligence tests in the white rat, and later that glutamic acid may have a facilitating effect on mental functioning in human subjects.

Glutamic acid was also shown by Weil-Malherbe to be the only amino-acid oxidized by brain slices.

Glutamic acid being an amino acid is also essential to liver function and the blood level of all amino acids is likewise affected by liver function.

Other liver-brain relationships may be more or less direct. Of all the vitamins, nicotinic acid appears to have the greatest effect on relieving toxic psychoses, not only in pellagrins, but in other malnourished patients not typically pellagrins. Nicotinic acid is essential, apparently, to normal methylation in the hepatic cells and repeated episodes of pellagra have been associated with the development of cirrhosis, other dietary factors obviously taking part.

The fact that severer cases of toxic psychosis may not respond as quickly to nicotinic acid has been cited as an argument that the needs of the liver must be met before those of the brain.

In any event, it is not clear whether the effect of nicotinic acid on the brain is direct or indirect, through liver metabolism.

Foster has shown that the detoxifying ability of the liver as measured by the benzoic acid-hippuric acid excretion test is diminished in severe toxic psychosis of long standing. He also demonstrated that the mental picture returned to normal only after improvement in this test of liver function. From his observations, Foster believes that "nutritional psychosis" is a better term than "toxic psychosis".

The nutritional state of hyperthyroidism, with its associated psychosis and liver function impairment, likewise bespeaks of a common denominator in the liver-brain relationship.

It has been suggested by Foster that the liver's role in brain function may be the synthesis of an intrinsic factor.

From a practical standpoint, I would urge, as have many writers, that patients with toxic psychoses be given

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500 mgm. of niacine daily, and I would suggest that any patient with toxic psychosis be considered to have impaired liver function until shown otherwise.

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Early Treatment for Children who Stutter.

Every preschool child who shows early signs of stuttering should receive immediate treatment, points out Dr. Isaac W. Karlin of the Speech Clinic of the Jewish Hospital of Brooklyn. (J.A.M.A., June 24.)

According to the author stuttering occurs in about 1 to 2 per cent of the population. The condition always begins in early childhood and is approximately four times as common among boys as among girls.

"A child of about three or four may begin to repeat words or sounds. He may show only an occasional slight hesitation in his speech and while speaking may stop suddenly as if groping for a word.

"There are no drugs today for the treatment of stuttering. The treatment is through the parents. The child's attention should not be drawn to his speech difficulty. In his presence the parents should talk in a simple, easy manner. They should not try to increase or improve his vocabulary. They should notice the situations or circumstances during which he talks best, and these conditions should be encouraged. Conditions under which he stutters more should be discouraged.

"Self-reliance should be encouraged, especially in eating and playing. A period of relaxation should be provided every day during which the mother reads to the child in a calm and easy manner.

"A question frequently is posed about the relationship between handedness and stuttering. There would appear to be no reason to believe that there is any. However, every child with a speech disorder should be encouraged to develop his dominant hand, be it left or right."

Mental Deficiency More Likely in Children Born to Mothers over 40.

Any woman who bears a child after the age of 40 runs a statistical chance of about 1 to 6 per cent of having a child with mongolism, a congenital mental deficiency.

This is brought out in a report by Dr. J. A. Book and S. C. Reed, Ph.D., of the University of Minnesota, Minneapolis, in the June 24, J.A.M.A.

Children with this severe condition commonly are called idiots. Mongoloid babies are recognized by their marked liveliness, flattened skull and oblique eyes.

The frequency of mongolism in the general population is estimated to be between 1 out of 500 and 1 out of 1,500, according to the report.

Risk of having a mongoloid child also increases after a mother has borne one baby with the deficiency.

"A woman who has borne a mongoloid child runs a statistical chance of about 4 per cent of having the next pregnancy result in the birth of another mongoloid child.

"This implies a 40 times greater risk than the average at all ages."

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TREATMENT OF LOWER NEPHRON NEPHROSIS BY INTESTINAL LAVAGE*

Myers H. Hicks, M.D.,
A. J. Crutchfield, M.D.,
and
J. Edwin Wood, M.D.,
Charlottesville, Virginia.

Lower nephron nephrosis as a cause of acute renal insufficiency is assuming increasing prominence as a medical problem. The common pathogenic factor seems to be a massive shock to the kidney. This may originate from a transfusion reaction, sulfonamide reaction, surgical shock post-operatively, post-abortion, after a crushing injury, in black water fever and a vast number of poisonings and other insults. The exact mode of mediation of this shock is not established, but Trueta[19,21] has demonstrated a shunt of the blood flow in the kidney. In this, the blood is deviated from the usual cortical path and instead is short circuited through the vasa recta and subcortical plexus. Others hold that the blood is pooled in the peripheral vessels[20] but the end result is agreed to be the same that is renal cortical anoxia. There is damage to the distal tubular segment of the nephron with subsequent necrosis and plugging of these tubules and resultant anuria[1].

The symptoms associated with this condition are, first, the symptoms of the pathogenic factor, and, second, anuria with its associated symptoms. It has been shown that in a majority of individuals with this lesion, regeneration of the tubular epithelium and spontaneous diuresis will ensue if the patient lives for ten to fourteen days. To insure the patient's chance for survival, certain measures are necessary. First, one must remove or correct the causative factor. Since no fluid is eliminated from the body save that by insensible loss or by defecation, the fluid intake of the patient must be sharply limited. The insensible loss of fluid is about 1,000 cc. per day. The preformed water and water of oxidation totalling 450 cc. daily is released, leaving a deficit of 550 cc. of fluid if the patient is completely anuric. One must replace this if concentration of electrolytes and cellular dehydration is to be avoided. Intake of protein and fat should be kept to a minimum to avoid rapid piling up of ketone bodies, urea and potassium. It has been shown[2] that by with-holding all nutriment from these patients except for 500 to 1,000 cc. of water containing 100 gms. of CHO, ketosis can be kept to a minimum and protein metabolism can be cut in half. By so doing urea formation and potassium liberation can be appreciably diminished. So favorably influencing the patient's metabolic processes makes his chances for remaining alive long enough to undergo diuresis appreciably greater. But one must repeat that restriction of fluid *per se*, thus preventing fatal edema and drowning of the patient is the prime consideration in his management.

In spite of this logical management, many of the patients will develop a metabolic situation with which we are primarily concerned in this presentation. Subjects with anuria who are not drowned by overzealous administration of fluid are still subject to elevation of the serum potassium and urea, as well as other metabolic products. It is known that many who die before diuresis die of cardiac standstill due to elevation of the serum potassium to a fatal level. The detection of potassium poisoning in an early stage is only possible by following the serum potassium and electrocardiographic changes at regular intervals.

In cases with potassium poisoning, some means of clearance of metabolic products must be instituted. Many methods for extra renal clearance of products of metabolism have been devised[3]. The general principle in all is similar, that is, migration of the metabolic products across a membrane into a lavaging fluid. We chose lavage of the stomach and upper small intestine because in our hands it is a simple and effective method[4,5]. (Fig. 1).

Materials and Methods: A Miller-Abbott tube is passed via the nose through the pylorus of the stomach two to five feet beyond into the small intestine.

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A Levine tube is simply inserted into the stomach, so the desired lavage fluid can be introduced through the Levine tube into the stomach. It passes down the intestine during which course substances with high concentration in the blood pass into the fluid. Constant suction is maintained on the Miller-Abbot tube and when the lavage fluid reaches the tip of this tube it is sucked back, evacuated from the bowel and thus eliminated with the waste products before absorption of appreciable fluids or electrolytes occurs.

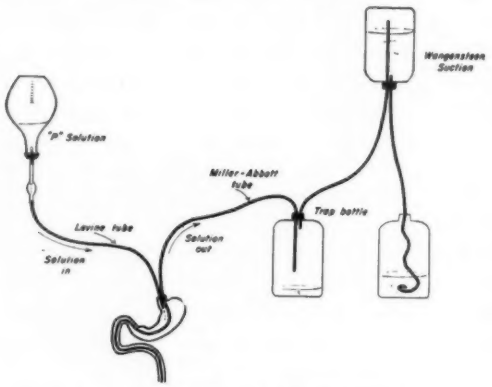

Fig. 1. Mechanism of intestinal lavage.

The solution used for lavage of the mucosa in this study was a modification of that already suggested[11]. It contained sodium chloride, sodium bicarbonate, calcium chloride and magnesium chloride in concentrations similar to plasma and glucose in concentration sufficient to supply the caloric requirement of the body as well as possible. (Table I).

	GRAMS/LITER
NaCl	6
$NaHCO_3$	3
$MgCl_2$	0.1
$CaCl_2$	0.1
Glucose	20

TABLE I. "P" SOLUTION

This solution was introduced through the Levine tube at a rate as near 10 liters/24 hours as possible. The solution was analyzed before and after passage through the tubing and bowel with determinations of urea, sodium, potassium, chloride, and volume. On occasions samples were obtained at five to six hour intervals and analyzed. The serum sodium was determined gravimetrically[14], and the urea, CO_2 combining power, and chlorides (plasma) by the conventional methods[15,16,17]. The serum potassium and the sodium and potassium in other fluids were measured by means of the Perkin-Elmer flame photometer.

One subject with acute renal insufficiency was treated for four days by intestinal lavage, and his case is reported below. Lavage was instituted in two subjects, one with chronic glomerulonephritis in its terminal phase, and one with malignant hypertension. This was done to prove the efficacy of the method.

RESULTS: CASE REPORT—LOWER NEPHRON NEPHROSIS

A 43 year old colored male was well until a frontal headache, persistent for 18 hours, necessitated his being seen in the clinic. While there, urine specimen was normal. He then had several generalized convulsions necessitating hospital admission.

On admission he appeared well nourished and of average size with normal blood pressure, pulse, respiration, and temperature. He was responsive only to painful stimuli and all reflexes were absent. The remainder of the physical examination was normal. The next day his temperature reached 104°F. and nuchal rigidity ensued. Sulfadiazine and penicillin therapy was instituted and about that time it was noticed that the urine volume was limited. The sulfadiazine was discontinued and streptomycin substituted. An indwelling catheter was inserted and urine volume remained below 50 cc. per day for five days. Fluid was limited to 750 cc. of 20 per cent glucose intravenously per day plus a volume equal to the previous day's urinary output. He developed a small amount of edema, but urine flow increased to 300 cc. per day on the sixth day. This urine was of 1.010 specific gravity and contained 36 mgm. per 100 cc. of urea and 1.5 grams of sodium chloride in the day's urinary output. Urine volume and constitution remained about this level for the next ten days. The blood urea had climbed steadily to a level of 292 mgm. per cent at this time and the CO_2 combining power had decreased to 10 m.Eq./liter in spite of administration of a portion of the prescribed day's fluid in the form of one-sixth molar sodium lactate on several occasions. The patient was stuporous and there was a "urea frost" on his brow. Heart rate was 50 and electrocardiogram showed changes characteristic of moderately severe hyperpotassemia[18]. (Fig. 2). There was auricular standstill with idioventricular rhythm. The QRS was 0.12 of a sec-

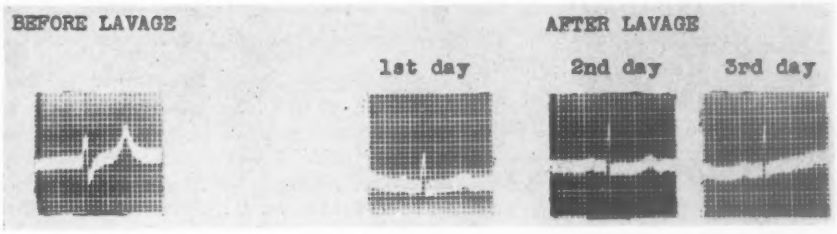

Fig 2. Electrocardiagram in patient with lower nephron nephrosis before and during lavage.

ond in duration and the T waves were tall and spiked. Tubes were passed for intestinal lavage, the Miller-Abbott tube being fed five feet beyond the pylorus. The first two days a solution of 0.9 per cent saline and five per cent glucose was used; then the modified "P" solution was utilized for lavage. Five to eight liters of fluid per day were passed through the system. After 24 hours of lavage an electrocardiogram showed the heart rate and rhythm to be normal with a QRS duration of 0.06 of a second and normal T waves. Later the CO_2 combining power and chloride became normal. The blood urea fell to 212 mgm. per cent. Because the serum potassium had fallen from 7.2 to 4.8 m.Eq./liter, lavage was discontinued on the fourth day of lavage and the nineteenth day of illness. No significant increase in edema occurred during the period of intestinal lavage. Blood chemistry values varied only slightly following this until the twenty-second day of illness when diuresis ensued. Even then the urine remained dilute, but the blood urea fell slowly and steadily. He became afebrile and asymptomatic, and was discharged on the thrity-fourth hospital day. (Table II).

	Before Lavage	During Lavage			
		1st day	2nd day	3rd day	4th day
Urea (mgm/%)	292	270	275	220	212
K (m.Eq./l)	7.2	---	---	---	5.2
Na. (m.Eq./l)	134	---	---	---	144
CO_2 (m.Eq./l)	10	12	12	22	21
Lavage Fluid		0.9% NaCl + Glucose		"P" Solution	

Table II. Blood chemistry changes during intestinal lavage in patient with lower nephron nephrosis.

This patient was slightly edematous and the small amount of sodium lactate he could tolerate did not alter his CO_2 combining power. After one day of lavage with "P" solution the CO_2 combining power increased from 10 m.Eq./liter to 22 m.Eq./liter. Potassium was removed in the fluid in a concentration about two-thirds to three-fourths that of the patient's serum level. The urea concentration of withdrawn solution was equal to blood urea concentration (292 mgm. per cent).

After two months, random urine concentration was 1.020 and P.S.P. excretion was 30 per cent in 15 minutes, 70 per cent in one hour, and the blood urea was 20 mgm. per cent. Blood pressure remained normal during the entire hospital stay and after discharge.

In the patients with hypertension and nephritis, the concentrations of urea and potassium in the lavage fluid were greater than one-half that of the concentrations in the blood serum. (Table III).

Discussion

The institution of upper intestinal lavage was not difficult. In all cases the method was in operation within three hours after attempts were begun. Two complications must be avoided. Pneumonitis is likely to develop but the use of prophylactic penicillin readily avoids this process. In all cases some fluid absorption is encountered. This must be kept to a minimum by careful supervision. Obviously the volume of fluid absorbed in a day must be subtracted from the day's proposed fluid intake. In the

			Solution Before Lavage		Solution After Lavage	
Patient	Bl. Urea (mgm/%)	Serum K (m.Eq./l)	Urea (mgm/%)	K (m.Eq./l)	Urea (mgm/%)	K (m.Eq./l)
1	292	7.3	0	0	292	3.9
2	274	5.4	0	0	156	3.9
3	120	3.0	0	0	60	3.0

Table III. Composition of perfusion fluid before and after lavage.

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subject with lower nephron nephrosis, 28 liters of fluid were used in lavage in the four days. Of this, 26.5 liters were recovered from the Miller-Abbott tube. Lavage of the stomach and upper intestine was preferred over other methods of clearance of metabolic products. It avoids the surgery, asepsis, mechanical difficulties and fluid absorption attendant on peritoneal lavage[6,7,8]. The artificial kidney is cumbersome and demands heparinization which is time consuming and difficult[9,10]. Colonic lavage results in decided fluid and electrolyte absorption[11].

As to its efficiency, as much as 18 grams of urea was removed in twenty-four hours of intestinal lavage. It has been shown that under basal conditions, removal of one to three grams of urea every twenty-four hours will afford a balance[4]. The role of urea, however, has been greatly over-rated[4,7,8]. It is true that the degree of urea retention is an indication of the degree of retention of other products of metabolism. However, oral administration of urea is associated with no significant toxicity[12,13].

We consider more important than this the fact that the subject with acute renal shutdown had hyperpotassemia that had progressed to a dangerous level. It had produced auricular standstill with idioventricular rhythm and a rate of 50 and a QRS complex of 0.12 of a second duration in the electrocardiogram. Lavage of the intestine for twenty-four hours resulted in reversion of the heart to a sinus rhythm with a rate of 68 per minute. The concentration of potassium in the lavage fluid averaged about ¾ of its concentration in the blood serum, and as much as 1.2 grams of potassium was removed in twenty-four hours of lavage. We would emphasize the necessity of repeated electrocardiograms and serum potassium determinations in the management of acute renal shutdown. This is necessary to decide when lavage must be instituted. We would also emphasize the hazard in acute renal insufficiency posed by hyperpotassemia and the efficiency of intestinal lavage in combating this hazard.

SUMMARY

1. The pathogenesis of lower nephron nephrosis is reviewed.

2. The logical management of this syndrome based on the pathologic physiology is outlined.

3. The importance of hyperpotassemia in acute renal insufficiency is emphasized.

4. Intestinal lavage is shown to be an effective means for extrarenal clearance of potassium and urea.

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DISCUSSION

DR. WALTER B. MARTIN, Norfolk: Doctor Wood's paper is of special interest in that he has pointed out the degree of potassium retention occurring in acute renal insufficiency with anuria, and has emphasized the part that this may play in causing cardiac deaths during such episodes. He has also demonstrated the possibility of correcting hyperpotassemia by lavage of the upper portion of the small bowel. Of particular interest is his third case, in which the serum potassium had accumulated to a high and dangerous level, and in which he was able to reverse this trend and restore the heart function to normal by intestinal lavage. Various methods have been proposed for combating the accumulation of dangerous substances in the blood in patients suffering from acute renal insufficiency, such as peritoneal lavage, with or without gastric lavage, exsanguinating transfusions, and the artificial kidney. The very fact that these rather difficult and laborious procedures have been introduced emphasizes the temporary nature of the syndrome that is commonly referred to as lower nephron nephrosis. The essential problem in this condition is to "tide the patient over" until the tubular damage can be repaired. This can be well understood, if we consider the nature of the condition. Acute renal damage, resulting in rapid onset of renal insufficiency, may occur as the result of a number of causes, such as shock from exsanguination, extensive burns, crush injuries, hemolytic transfusion reactions, and chemical poisoning. The lower segment of the nephron is the location of the greatest damage. The lining cells of the tubules undergo necrosis and the tubule takes on the attributes of a dead membrane. Filtration from the glomeruli may not be materially affected, but unhibited absorption of this filtrate by the tubule may result in complete anuria, lasting for days. Recovery from this condition depends upon regeneration of the lining cells of the tubules, and the restoration of their normal selective, absorptive function. In complete anuria, there is a rapid building up of toxic substances in the blood. It is estimated that natural repair of the tubules may take place in eight to twelve days, if the original cause of the injury ceases to operate. It is evident, then, that measures designed to remove these substances by extra renal routes are of great potential value. If these substances can be kept below the critical level for a relatively short period of time, the patient may recover by natural processes. Without going into discussion of the mechanism by which the tubular damage may be accomplished, it might be well to point out two phases of treatment. The initial phase of shock must be combated with suitable blood substitute, in a case of severe blood loss or destruction by whole blood, or in extensive burns, by plasma. This must be accomplished in sufficient volume and with sufficient speed to restore blood volume, and blood pressure to a suitable level as rapidly as possible, so as to minimize the extent of the renal damage. There is little evidence that the kidney lesion is progressive, once a proper circulatory mechanism is restored, and acidosis prevented or controlled. From that point on, as has been emphasized by Dr. Wood, great care must be taken to maintain a proper water balance. The first phase may change rather abruptly to the second, and keen clinical judgment is needed at this point. Van Slyke has pointed out the value of the copper sulphate falling drop method in estimating the specific gravity of the blood and the use of this as a guide in determining the proper level of fluid intake. The copper sulfate method of Van Slyke was of great value on the battlefront in dealing with the numerous cases of shock resulting from burns, crush injuries, dehydration and exsanguination. It made possible a rapid calculation of the amount of blood substitutes needed in each case. During the period between the restoration of the circulatory function and the recovery of the damage to the renal tubules, the problem becomes one of maintaining the nutrition of the patient, and a normal water balance, and the removal, by extra renal routes, of toxic accumulation. It is in this field that Dr. Wood's contribution is most valuable.

DR. J. EDWIN WOOD, JR., Charlottesville: Dr. Hicks has done a great deal of detail work on this subject, and I am sure would like to tell you a good deal more about our findings. I should like to mention one or two other things in which we are interested.

Dr. Martin has said, "When you get to the right point stop there and don't go any further." He is right. It is quite true that you can drown anuric patients, and rather easily, by the over-administration of fluids. I am quite sure that many present will remember the time honored thought that the best way to make the kidney put out urine was to force fluids intravenously. Like so many generalizations, this does not fit certain specific cases.

The literature calls attention to the fact that the stomach fluids contain potassium. We thought maybe a good way to treat potassium poisoning was by washing out the stomach instead of the intestine, but it is not an adequate method. The wall of the intestine is a semipermeable membrane and is the best available structure of its kind for extra renal clearance by lavage.

As Dr. Hicks showed you in his paper, the concentration of sodium in the perfusion fluid remained approximately the same as in the blood, but as there was no potassium in the perfusion fluid, this substance came out in fairly large amounts.

A MEMBER: I should like to ask a question of Dr. Hicks. I am interested in how they keep the intestine

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from riding up on the inflated balloon. I know in chronic ulcer and colitis you have a great difficulty in keeping the balloon blown up. If you deflate the balloon you see the fluid go beyond the point of suction, which defeats the purpose. I am interested in knowing how they handle the situation.

DR. HICKS, closing the discussion: We did deflate the balloon, so the tube would not progress on down the bowel. We recovered 26.5 out of 28 liters of the lavage fluid in one individual which was very satisfactory. I do not know whether or not this success was due to the speed at which we administered the fluid, but this must be a factor. One patient developed diarrhea, and that was thought to be due to the lavage fluid reaching the lower bowel in appreciable quantities, so such successful recovery of lavage fluid was not always possible.

I should like to thank Dr. Martin for his valuable discussion of this problem.

Deaths from Influenzal Meningitis Almost Eliminated by Drugs.

A recovery rate from influenzal meningitis of 96 per cent following treatment with sulfadiazine and streptomycin is reported by Drs. Emanuel Appelbaum and Jack Nelson of the New York City Health Department in the June 24 J.A.M.A.

Before the use of sulfa and antibiotic drugs, the mortality from the disease varied from 90 to 100 per cent.

The authors further state that this form of meningitis (an inflammation of the membranes that envelop the brain and spinal cord) is essentially a disease of infants and young children. Of 90 patients treated, 87 recovered and three died. In the vast majority of these patients, there was marked improvement in six days after treatment with streptomycin was begun.

Residual damage, including deafness and defective vision, occurred in nine of those who survived.

Reports Development of Laboratory Tests for Diagnosis of Virus Diseases.

Development of practical laboratory tests for diagnosing virus and rickettsial diseases is reported by a Chicago doctor in the May 20 *J.A.M.A.* The tests were used on 349 patients, Dr. Albert Milzer of the Medical Research Institute, Michael Reese Hospital, says.

According to the author: "In the past, laboratory techniques for diagnosis of the virus and rickettsial infections have been too complicated for the routine hospital laboratory."

"These procedures were largely limited to research laboratories. Recently tests for many of these diseases have been developed to the point that hospital laboratories can perform many of these tests and be of great diagnostic aid.

"The fact that virus and rickettsial diseases such as psittacosis [parrot fever], influenza and Q fever may closely simulate a typical [not characteristic] pneumonia serves to emphasize the diagnostic value of conducting serologic tests for patients with infections of the respiratory group.

"Furthermore, the full benefits of chemotherapy are more apt to be achieved if the exact basis of the disease is known."

The procedures reported do not include a satisfactory routine laboratory test for poliomyelitis.

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Medical Society of Virginia Cancer Committee

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AUGUST 1, 1950

Case Reports

A 42-year-old woman discovered a hard lumpy area several cm. in diameter in the skin of her right breast. Fearing cancer, she at once consulted her doctor who told her he did not think she had cancer but to come back if she had further trouble.

Five months later after a strain, pain severe enough to limit her activities developed in the lower back, right hip and leg. Her doctor and his associate now both examined her. The lumpy area in the skin of the right breast was definitely larger, but they felt that it was insignificant and attributed her back pain to a uterine mass, for which they advised hysterectomy. This she refused. After seven months of gradually increasing pain, an X-ray examination of the spine revealed destruction of the third lumbar body. This was interpreted as representing hemangioma, a back brace was prescribed, and hysterectomy again advised and refused.

When the strap of the back brace irritated the lumpy area in the skin of the right breast, the patient consulted a dermatologist. He at once referred her to a surgeon who found a large hard tumor underlying and attached to the thick, puckered, dark skin area. In addition to the uterine mass (probably a fibroid), there were hard nodes in both axillae. A biopsy specimen from the breast lesion revealed carcinoma. Roentgenograms showed metastases in the pelvis, upper femurs, and in many vertebrae and ribs. The third lumbar body was badly collapsed.

Comment: 1. Three physicians, two general practitioners and a roentgenologist, failed to think of cancer as a diagnostic possibility when presented with a breast tumor invading the overlying skin and a destructive, painful bone lesion.

2. As a result, the diagnosis was not reached until one year after it should have been made; the patient lost all chance for a cure (the survival rate following radical mastectomy for cancer without demonstrable metastases is 75 per cent; for cancer with demonstrable metastases in the axilla only 25 per cent); she was allowed to suffer from painful bone metastases without the relief of palliative radiation and hormonal therapy for seven months.

3. Discovery of a breast mass is a medical emergency, demanding the immediate attention of a surgeon capable of performing a radical mastectomy should cancer be found at biopsy.

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SARCOIDOSIS*

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The riddle of sarcoidosis, or the sarcoid of Boeck, remains unsolved after fifty years of observation, study, and research. However, the efforts of investigators in the past have not been too strenuous because the disease was thought to be rare, as well as having a low mortality. Recently, with the advent of X-ray surveys and the routine X-ray examination of all armed service personnel on induction and discharge, many cases otherwise unsuspected were found.

This survey and study comprise cases diagnosed in a general Veterans Administration Hospital and in two general civilian hospitals. A total of thirty-eight patients have been studied. The full initials of the cases will be used, as it is probable that the same patients have been, or will be, reported from other hospitals in later studies. The benign course of sarcoidosis makes this a definite possibility. In fact, two of the cases studied here have already been reported in the literature.[1]

The original description by Boeck[2] of a disease of the skin characterized by nodular and infiltrative lesions, which showed on microscopic examination epithelioid tubercles without caseation, has now been modified to include the invasion of all of the body tissues by these hard tubercles. Many authors have stressed the fact that this disease is systemic and protean in nature and should be properly called sarcoidosis rather than sarcoid. Chart I shows the distribution of involved tissues in our cases.

Chart I
Sarcoidosis — Statistics
38 Cases
Average age for group—27 years.
Youngest—19 years. Oldest—66 years.

Negro patients	33	87%
White patients	5	13%
Male* patients	37	97%
Female patients	1	3%
Tissues Involved (Multiple)		
Lungs	28 patients	74%
Glands	25 patients	66%
Eye	16 patients	42%
Skin	10 patients	26%
Bone†	2 patients	5%
Nervous System	4 patients	10%
Spleen	2 patients	5%
Mucous Membranes (nose)	3 patients	8%
Heart	1 patient	3%
Liver	1 patient	3%
Tissues Involved (Single)		
Lungs	7 patients	18%
Skin	1 patient	3%

The current literature contains reports of nearly two thousand cases; and when one includes such conditions as uveoparotid fever (Heerfordt's disease), granuloma of lacrimal glands (Mikulicz's disease), subcutaneous infiltrations (lupus pernio), cystic formation of bones (Jungling's disease), and regional ileitis, the number is increased several fold. These are now considered by many to be forms of sarcoidosis.

Several theories as to the etiology of sarcoidosis have been considered since its discovery as a clinical entity. Pinner[3] expressed an opinion in which we concur; he said, "no one has been able to prove his theory convincingly, even to his own complete satisfaction." However, it seems that the majority favor the tubercle bacillus, or its products, as the

*Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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Read before the annual meeting of the Medical Society of Virginia, at Fort Monroe, October 9-12, 1949.

*Most of cases came from Veterans Administration Hospital having only male cases.

†Very few cases had X-ray of bones unless there was a specific complaint.

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causative agent in patients, with high immunity and low sensitivity. Other theories include the non-specific response of tissues to various micro-organisms; a virus infection causing a chronic granulomatous response, and a pathological entity similar to Hodgkin's disease. Meyer[4] has recently given an excellent review of this problem in which he points out the evidence incriminating the tubercle bacillus. Freudenthal[5] also gives further indirect proof in a recent pathological study.

The symptoms of sarcoidosis are characteristically bizarre and non-specific. Even with extreme pathological changes these may be minimal or absent, especially when the skin, lymph glands, and lungs are involved. The exceptions are lesions of the eye, involvement of the cranial nerves, and the central nervous system.

In the series of cases studied, the following symptoms were noted: weakness, pain in back, legs, abdomen, joints; anorexia and weight loss; eye pain and disturbance of vision; lacrimation; redness of eyes; fever (low grade); cough; dyspnea; tachycardia; muscle twitching; paralysis; swelling of joints, also fingers, hands, and toes; hemoptysis; mental confusion; "lumps" on the skin; vertigo; nausea and vomiting. These symptoms showed a tendency to regress when the disease became inactive, unless function of organs or nerves was destroyed.

The findings in sarcoidosis may be minimal, as a few scattered skin lesions on the trunk, face or arms; or one may note palpable lymph nodes, either cervical, axillary, or inguinal. These glands are firm, movable, and painless. Occasionally, the X-ray film will reveal paratracheal and hilar adenopathy or diffuse nodular densities. These are usually "picked up" on routine physical examination or in the course of diagnostic procedures for other disease conditions. Not infrequently the pathologist, surprisingly, will report sarcoid tubercles in routine tissue examinations. On the other hand, as would be expected, occasionally marked symptoms and definite signs cause the patient to seek medical treatment for this as a primary condition. In our series, seven patients (18%) gave no symptoms and three (8%) had irrelevant complaints. The remainder of the group gave one or more of the previously mentioned symptoms.

As has been noted by Reisner[6] and others, the majority of the cases occurred in Negroes (87%) with males predominating. The sex ratio is not significant as most of our cases were from a Veterans Hospital not admitting females. The average age was twenty-seven years with the youngest nineteen and the oldest sixty-six years.

The clinical laboratory has not been too helpful in aiding or confirming the diagnosis when sarcoidosis was suspected. The usual observations in this condition have been adequately reviewed by Freiman.[7] These consist of a moderate monocytosis and an occasional eosinophilia. The sedimentation rate is usually elevated but does not parallel the activity of the disease process. In our series seventeen had elevation of their rates out of twenty-six tested (or 65%). The total protein may be increased above eight grams per 100 c.c., but out of thirty-two examinations only five (16%) showed a significant increase. A reversal of the A/G ratio has been a more consistent finding. Nineteen patients out of thirty-two (58%) showed a reversal. Twenty-six patients had sputum examinations and these were all negative. A tuberculin test was done on twenty-seven patients with three positive reactors. Two negative reactors (cases R.M.H. and D.E.) later became positive and had a clearing of the signs of sarcoidosis in their chests.

An X-ray film of lungs gives the best evidence in suspecting sarcoidosis, and, as pointed out at the beginning, has led to the discovery that this disease is not as rare as was suspected a decade ago. Plates I

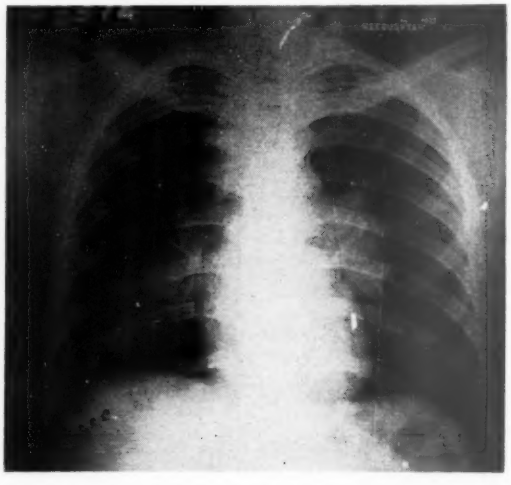

Plate I. Case 27—JCP. Marked degree of bilateral hilar and right paratracheal adenopathy (potato nodes).

Plate II. Case 11—CJF. Diffuse symmetrical, parenchymal nodular infiltration.

and II show films of sarcoid lesions in the chest. Garland[8] has very clearly described these early roentgenological findings. Charts II and III give the roentgenographic criteria and differential diagnosis. But, with this fairly clear X-ray pattern of the disease, everyone is agreed that films are not pathognomonic. Even when an associated bone lesion is found, one still cannot be too confident of the diagnosis. Plates III and IV show typical bone and skin lesions. Chart IV shows the typical findings in the skin and eye.

CHART II

SARCOIDOSIS—X-RAY CRITERIA

PULMONARY

The pattern is variable as to character, extent, distribution, and is not pathognomonic. These findings in order of frequency are:

1. Bilateral hilar and right paratracheal adenopathy with or without associated parenchymal infiltration. The glands are discrete and show a lobulated border because of over-lapping. This pattern is an extremely valuable roentgenographic sign.
2. Diffusely disseminated changes consisting of discrete miliary or nodular densities, without calcification, in a patient who is clinically well.
3. Diffuse or localized linear or strand-like densities following the broncho-vascular radicles. This results in prominent root and peripheral shadows.
4. Massive hilar node enlargement (potato node) in a person who presents no complaints.

Differential Diagnoses:

Miliary tuberculosis; Hodgkin's disease; silicosis; hemosiderosis in mitral valve disease; coccidiosis; erythema nodosum; vascular congestion; lymphangitic carcinosis; lymphosarcoma; mycotic infection; beryllium pneumonitis and granuloma.

CHART III

SARCOIDOSIS—X-RAY CRITERIA

BONE

There is a predilection for the small bones of the hands and feet. The process begins in the medullary cavity and is difficult to detect until there is cortical involvement.

1. "Punched out" lesions with no local reaction in adjacent bone.
2. When perivascular infiltration of Haversian canals occurs, destructive changes in the cortex result in a reticular "lace-like" pattern with or without pathological fracture.
3. May have a combination of 1 and 2.
4. Occasionally, in a rapidly expanding lesion, there will be destruction of a portion of bone.
5. The periosteum is not involved and the joint space is intact; therefore, there is very little impairment of function.

Differential Diagnoses:

Hyperparathyroidism (osteitis fibrosa cystica); polyostotic fibrous dysplasia; multiple enchondromata; gout; rheumatoid and hypertrophic arthritis; fungus diseases; syphilis; neurotrophic changes; tuberculous dactylitis; cartilaginous "rests"; and xanthofibroma.

Plate III. Case 15—BRH. Irregular cystic areas of rarefaction with multiple pathological fractures of the phalanges.

CHART IV

SARCOIDOSIS—SKIN LESIONS

1. The superficial type (Besnier-Boeck) is varied in appearance. It may be macular, plaque, disseminate nodules, both small and large. Larger nodular lesions often have a flattened surface which sometimes may

Case No.	Initials	Age Sex Race	Symptoms	Org. Inv.	X-ray	Biop Sy	TBN	A/G	Sed. Rate	Miscellaneous Findings	Present condition	Duration Mos.	Case No.
1	MA	21MN	None. (Routine X-ray of chest).	L,G	L+	G+	n.d.	1.8	norm.	Sputum−.	1949. Asymptomatic.....	35	1
2	SDA	26MN	None. (Routine X-ray of chest).	L,G	L+	G+	−	3.0	elev.	Sputum−. Tbc.+ and Tbc. adenitis at 3 yrs. of age.	1949. Asymptomatic.....	72	2
3	EA	23MN	Productive cough and chest pain.	L,G	L+	n.d.	2nd+	rever.	elev.	Sputum−. Hookworm ova in stool.	1947. Asymptomatic. X-ray of chest unchanged.	45	3
4	BBB	26MW	Tachycardia, weight loss, fever.	L,G, B,H	L+ B+	G+	−	1.9	n.d.	Sputum−. TP 8.0.	1949. Dyspnea on exertion, ataxic gait, tachycardia.	76	4
5	CAB	22MN	Syncope, night sweats, fever, weight loss, anemia, dyspnea, swelling of eyelids.	L,E	L+	n.d.	−	2.8	elev.	Sputum−.	1947. X-ray showed advanced Tbc. of left lung. Guinea pig inoculation was +. 1949 symptomatic.	61	5
6	SB	22MN	Chest pain.....	L	L+	n.d.	−	0.8	n.d.	Sputum−. Sister has same condition.	1947. Cough, weakness, dyspnea. X-ray of chest unchanged.	7	6
7	JRD	30MN	None. (Routine X-ray of chest).	L,G, NM, CNS, E	L+	G+	−	0.5	norm.	.....	Died 1948 of Tbc. meningitis with abscesses of psoas muscle, groin, and brain.	12	7
8	WHE	49MN	Twitching eyelid, throbbing in throat.	L,CNS	L+	G−	2nd+	1.8	n.d.	Gastric washing −.	Died 1947 with convulsions. NP consultation showed a cerebral lesion. No autopsy.	7	8
9	DE	21MN	Anorexia, eye pain, dizziness, weight loss, pain and swelling of joints.	L,G,E	L+	G−	+	1.2	elev.	Kahn+.	1947. Marked eye symptoms. X-ray chest−, Tbn.+. Treated with Tbn. and Typhoid vaccine. 1949 chest X-ray−.	39	9
10	HF	22MN	Chest pain, cough, blood streaking, weakness, fatigability	L,G	L+	G+	n.d.	0.9	norm.	Sputum−.	1947. X-ray of chest−.	31	10

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11	OJF	27MN	Pruritus, drowsiness, precordial pain, nervous stomach, cough, weight loss.	L,G,S	L+	S+	n.d.	n.d.	n.d.	.....	1949. X-ray of chest−. Tbn.−. Sed. Rate normal. Nodule from epididymis+.	13	11
12	HG	23MN	Cough and weight loss.....	L,G	L+	n.d.	−	1.4	elev.	Kahn+. Sputum−.	No follow up.....	0	12
13	FHH	30FW	Weakness, cough, hemoptysis, fever, anorexia, weight loss.	L,S	L+	S+	−	0.9	elev.	Sputum−. Renal lithiasis.	Died 1947 in pulmonary failure.	48	13
14	LBH	23MN	Eye pain, chest pain.....	E,Sp., Li	L−	n.d.	−	1.1	n.d.	Left eye enucleated.	1949. Asymptomatic. Chest X-ray−.	48	14
15	BRH	48MN	Pimple on nose. Swelling of finger.	L,B,S, E,NM	L+ B+	n.d.	n.d.	2.3	n.d.	.....	1947. Unchanged.....	31	15
16	RMH	25MN	None. (Routine X-ray of chest).	L	L+	n.d.	−	2.5	norm.	Sputum−. Kahn+.	1947. Weakness and palpitation. X-ray of chest−. Tbn.+. Kahn+. 1949 many colds.	39	16
17	LTH	23MN	Weight loss. (Routine X-ray of chest).	L	L+	n.d.	−	norm.	norm.	.....	1947. X-ray of chest−.....	15	17
18	WHH	20MN	Watering and pain in eyes, swelling of glands, skin bumps.	L,G,S, E	L+	S+	−	3.8	elev.	Sputum−. Kahn+. Rt. eye enucleated.	1946. X-ray unchanged. Tbn.−. Skin biopsy+.	23	18
19	LH	20MN	Pain in stomach, chest, neck; vomiting, cough.	L,G,S	L+	G+	−	1.4	norm.	Sputum−.	1949. Same symptoms. X-ray chest 1948 unchanged.	48	19
20	PEJ	38MN	Swollen glands, back pain, weight loss, weakness, chills, fever.	L,G,E	L+	G+	−	0.6	n.d.	.....	No follow up.....	0	20
21	JEJ	22MN	Back pain, eye pain, swelling of neck and wrists, fever, headache, night sweats, dyspnea, dizziness.	L	L+	n.d.	n.d.	0.8	elev.	.....	1947. X-ray of chest unchanged.	7	21
22	JWL	35MW	Pain in hips, shoulders, knees.	L	L+	n.d.	n.d.	n.d.	n.d.	Sputum−.	No follow up.....	0	22
23	GM	26MN	Dyspnea, bumps on skin....	L,G, Sp.,S, E	L+	S+	−	3.6	elev.	Sputum−. TP 8.4. Kahn+.	1949. Heart enlarged. Infiltration rt. apex. CNS syphilis.	68	23
24	MN	22MN	Weakness, discomfort in eyes. (Routine X-ray).	L,G,E	L+	G+	n.d.	2.5	n.d.	Sputum−.	1949. Asymptomatic.	80	24

Case No.	Initials	Age Sex Race	Symptoms	Org. Inv.	X-ray	Biop Sy	TBN	A/G	Sed. Rate	Miscellaneous Findings	Present Condition	Duration Mos.	Case No.
25	JMM	66MW	Asthma.....	L	L+	n.d.	–	0.8	elev.	Sputum–.	Died 1949 of Hypertensive Arteriosclerotic ht. disease with pul. emb. and infarct.	40	25
26	WN	23MN	Mental confusion, convulsions, bumps on skin, swelling of fingers; eye discharge.	G,S,E, CNS	L–	G+	–	0.6	n.d.	.....	Received HN_2 therapy. 1949 developed tbc. pneumonia. Sputum+.	57	26
27	JCP	26MN	Nausea, anorexia, back pain.	L,G	L+	G+	–	2.1	norm.	Sputum–.	1949. Unchanged.....	4	27
28	LTR	27MN	Anorexia, fatigue, wt. loss, cough, skin bumps.	L,G,S	L+	S+	–	1.3	elev.	Sputum–. Inv. T,CF4.	1949. Back pain and chest pain.	48	28
29	OR	24MN	Pain and redness of eyes....	L,G,E	L+	n.d.	n.d.	n.d.	n.d.	Left eye enucleated.	1945. X-ray of chest unchanged.	22	29
30	AGS	26MW	Fever, chills, chest pain, rusty sputum, cough, weakness, weight loss.	L	L+	G–	–	1.4	norm.	Sputum–. Yeast organism in sputum. Treated with KI and monilia vaccine.	.....	40	30
31	NS	23MN	Burning eyes, knots in eyelids, stomach pain, vomiting.	L,G,E	L+	G+	n.d.	n.d.	n.d.	Left eye enucleated.	1946. Unchanged.....	65	31
32	JHS	23MN	Cough, dyspnea, chest pain, lumps in skin.	L,G,S	L+	G+ S+		0.3	elev.	Sputum–. Mother died of Tbc.	1943. Unchanged.....	13	32
33	CDT	19MN	Chest pain, tachycardia, diminished vision, vertigo, headache, swelling of ankles.	L,G,E	L+	n.d.	–	n.d.	n.d.	Sputum–.	1948. Same symptoms. X-ray of chest negative.	39	33
34	EWW	21MN	Cough, chest pain, weakness, wt. loss, loss of smell, fever, itching, painful joints, paralysis, warts on penis, anus, face.	L,G,S CNS	L+	G+ S+	–	1.2	elev.	Gastric wash.–. Twin of case 35.	1949. Dim vision. X-ray unchanged.	51	34

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35	JBW	21MN	Chest pain, dyspnea, epistaxis, hemoptysis, swelling eyelids, painful parotids and testicles, swelling of ankles and legs, constipation.	L,G,E NM	L+	G+	–	0.9	elev.	Sputum–. Brother of case 34.	Died 1949. Had received HN_2 therapy. Developed bone and pulm. Tbc. and died of Tbc. meningitis.	32	35
36	REW	21MN	Chest pain, cough, photophobia and blurring of vision.	L,G,E	L+	G+	n.d.	1.0	n.d.	.....	1949. Unchanged.....	42	36
37	RW	49MN	Fatigability and skin lesions.	S	L–	S+	n.d.	1.5	elev.	Sputum–.	1948. Fusion of spine for Tbc. X-ray of chest–.	51	37
38	FY	20MN	Redness of eyes.....	L,G,E	L+	G+	–	1.1	n.d.	1° A.V. Block.	1947. Difficulty in vision...	42	38

TABLE I—LEGEND: B—bone; CNS—central nervous system; E—eye; elev.—elevated; F—female; G—lymphatic glands; H—heart; L—lungs; Li—liver; M—male; N—Negro; n.d.—not done; norm.—normal; NM—nasal mucosa; Org. Inv.—organs involved; Sp.—spleen; Tbc.—Tuberculous; Tbn.—tuberculin; W—white; +—positive; –—negative; 2nd—2nd strength.

Plate IV. Case 32—JHS. Superficial flattened nodules, of varying size, involving the back and arm.

be loculated. Occasionally, an annular type of sarcoid is present with central atrophy. Ulceration is rarely seen. The color is often that of the skin, but at times may be bluish-brown or purplish red. On diascopic pressure the small yellowish nodules do not completely blanch. In the colored race there is occasional depigmentation.

2. The deep type (Darier-Roussy) consists of subcutaneous nodules, not infrequently resembling erythema induratum.
3. The above lesions may also occur on the mucous membranes, especially in the nose.

Differential Diagnoses:

Lupus erythematosus; tuberculosis cutis; late nodular syphilis; leukemia cutis; adenoma sebaceum; xanthoma; multiple keloids; leprosy; erythema nodosum; erythema induratum; granuloma annulare; nodular and cystic acne; and paraffinoma.

SARCOIDOSIS—EYE LESIONS

Eye involvement may be a most serious manifestation of the disease, often causing the loss of the eye or impairment of vision. Invasion of the optic nerve is usually associated with sarcoidosis of the brain. The following conditions are usually noted:

1. Iritis or iridocyclitis.
2. Nodules of the cornea with opacities.
3. Synechiae and glaucoma.
4. Retinitis and choroiditis.

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It then follows that the positive final diagnosis of sarcoidosis rests on the microscopic examination of tissue. Here one has also to be careful, for often a foreign body reaction will produce hard tubercles in a person whom one feels certain does not have sarcoidosis. In reviewing material and case histories for this paper, one patient was found with a sarcoid-like lesion resulting from a lip injury caused by a dental drill. Another case, having active pulmonary tuberculosis, was operated on for an acute appendicitis. On pathological examination this was found to be a sarcoid lesion of the appendix. They had no other evidence of sarcoidosis and were not included in the series.

The histological findings in sarcoid are characteristic and, when linked with signs of multiple involvement of tissues, the diagnosis is evident. The pathological picture of these hard tubercles shows a collection of large epithelioid cells with occasional giant cells and no caseation. There is no surrounding halo of lymphocytes, no organisms are ever found, and, even in large clusters, the tubercles do not become confluent. The findings are uniform in all tissues. Stone[9] has emphasized the absence of inflammatory changes and the marked tendency to fibrosis. The Kveim test is helpful, though not always accurate, and is a technically difficult procedure.

Once the diagnosis is made, one is then confronted with two problems, the treatment and prognosis. Therapy of this disease, in the past, has not been too satisfactory. Results are often confused by the spontaneous regression of the demonstrable pathology and the lack of specific symptoms. In fact, one may state that the search for a specific therapeutic agent has been as fruitless as the discovery of the etiologic agent.

Most men today treat the symptoms only when function is impaired, hoping that the course will be benign, as it usually is, and that no vital structures will be involved.

In our series no attempt at specific therapy has been made. Rest, nourishing food, adequate vitamins and essential minerals are the best treatment to date. Many cases develop tuberculosis, in our group eleven per cent, so the rationale of this is evident. A recent series treated with calciferol and dihydrotachysterol by Curtis and Grekin,[10] while impressive, has had too short a follow-up for a disease with the tendency to spontaneous regression. Snider[11] has used nitrogen mustard with no conclusive benefit; in fact, one patient, an identical twin (J.B.W.), became worse after treatment. He later developed bone and pulmonary tuberculosis and recently died of tuberculosis meningitis. The other twin (E.W.W.), untreated, has remained well.[1] A recent personal communication from Jones[12] reports on the use of urethane. He has been impressed by the results but the follow-up period has been too short for definite evaluation.

Now, mostly abandoned, is the use of antileprol, arsenic, bismuth, gold, radium, tuberculin, ultraviolet light, and X-ray therapy.

There have been no series reported which used penicillin, Aureomycin, chloromycetin or para aminosalicylic acid.

The follow-up period in our series has ranged from one visit to eighty months, with an average of thirty-five months. As has been noted by others, most of the patients are living and well. Some have more X-ray evidence of progression than symptoms, and unless each patient is completely surveyed on follow-up this will be missed. Several have developed tuberculosis—in our series eleven per cent. Others have become crippled with pulmonary insufficiency. Five have died, giving a thirteen per cent mortality. In spite of this, one can usually give a fairly good prognosis. It has been our impression that anything which tends to break down the natural resistance of the body has a definitely unfavorable effect on the prognosis. Table I is a composite picture of all cases.

SUMMARY

1. Thirty-eight cases of sarcoidosis have been studied and reviewed.
2. We found sarcoidosis more common than it had been thought to be; many cases were picked up on routine X-ray films. It occurred mainly in young adult negro males.
3. The etiology is unknown. The relationship to the tubercle bacillus or its products has not been clarified, but we feel as many others that there may be a common etiological agent.
4. Symptoms may be absent or minimal even with fairly wide-spread disease.
5. It is a generalized disease involving many structures and organs.
6. There are no specific laboratory findings.

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7. X-ray films of the chest and bones, although suggestive, are not pathognomonic.
8. The diagnosis is made by exclusion, after review of the history, physical examination, laboratory findings, and X-ray films. If, in addition, biopsy of tissue is characteristic and there is multiple involvement of organs, the diagnosis is fairly certain.
9. There is no specific therapy. The lesions may regress spontaneously in a variable period of time.
10. The prognosis should be guarded. Several cases developed tuberculosis and died; others required enucleation of an eye, and some developed chronic pulmonary insufficiency.

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Fermentation Drug Combats Eye Infections.

Successful treatment of eye infections with sodium propionate, a drug derived from a substance produced in a fermentation process, is reported by Dr. Frederick H. Theodore of Mount Sinai Hospital and the Manhattan Eye, Ear and Throat Hospital *J.A.M.A.* for May 20.

The drug is effective against all the bacteria causing common eye infections and against fungi.

He states that clinical results in some 1,200 patients treated with sodium propionate appear to be as good as those obtained in acute eye infections by treatment with any of the newer antibiotic drugs.

Sodium propionate appears to be a useful supplement to the antibiotic drugs and sulfa drugs, which in some eye infections often prove to be of little permanent value because of the development of bacterial resistance and drug sensitivity, he indicates. Results from use of sodium propionate in these conditions are gratifying.

The fact that sensitivity to the drug is rare makes it an especially valuable agent in infections in allergic persons or in cases in which drug sensitivity already has occurred.

XUM

PREINVASIVE CARCINOMA OF THE CERVIX: AN OPPORTUNITY TO REDUCE CANCER MORTALITY*

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Though cancer of the cervix is one of the cancers most amenable to treatment, the rate of cure is far from satisfactory. It is probable that less than 30 per cent of all women treated in the United States for cancer of the cervix are alive and free from the disease at the end of five years. This rate is too low for cancer in an easily accessible non-vital organ. Without question, with our present knowledge, it can be improved.

Deaths from cancer can be decreased by prevention, improved treatment, and earlier diagnosis. At this time we know too little about the causation of carcinoma of the cervix to accomplish much more in its prevention; and there is no foreseeable improvement in the technique of present methods of treatment which can be expected to lower the mortality greatly. However, right now much can be accomplished by earlier diagnosis. The importance of early diagnosis is illustrated in Table I which shows how the cure rate drops as the disease advances:

TABLE I
FIVE-YEAR CURE-RATE BY STAGES
LEAGUE OF NATIONS REPORT

	Per cent
Stage I	57.2
Stage II	37.6
Stage III	22.0
Stage IV	5.5
All Stages	27.6

Despite the time which has elapsed since these figures were published, they remain essentially true for results today. Therefore, it is a tragedy that even now the majority of patients are being first treated late in the disease. Figure 1 shows the stage distribution of cases first treated at the Medical College of Virginia during the ten year period 1934-1943. In only 10 per cent of the cases were the lesions grossly confined to the cervix.

*Read at the annual meeting of the Medical Society of Virginia, at Fort Monroe, October 9-12, 1949.

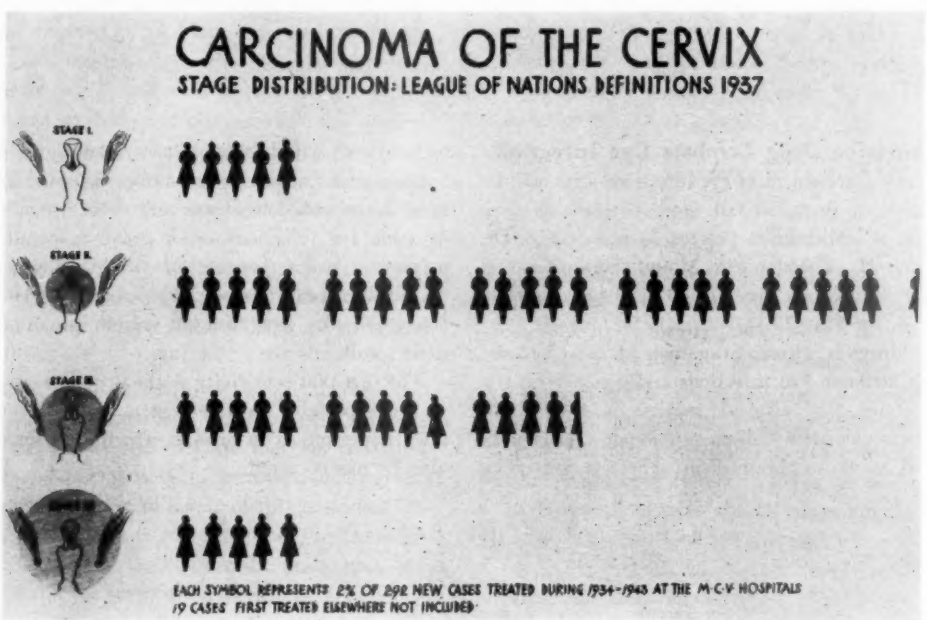
CARCINOMA OF THE CERVIX
STAGE DISTRIBUTION: LEAGUE OF NATIONS DEFINITIONS 1937
STAGE I.
STAGE II.
STAGE III.
EACH SYMBOL REPRESENTS 2% OF 298 NEW CASES TREATED DURING 1934-1943 AT THE M.C.V. HOSPITALS
19 CASES FIRST TREATED ELSEWHERE NOT INCLUDED

Fig. 1.

There are many laudible and promising activities aimed at bringing about earlier diagnosis of *invasive* carcinoma of the cervix, but so long as we maintain that existing invasion is essential to the diagnosis of cancer, we miss the opportunity to diagnose and treat truly early carcinoma.

The concept that carcinoma is at first intra-epithelial and for the time non-invasive is not new. In 1912 Kermauner and Schottländer described changes in surface epithelium adjacent to invasive carcinoma of the cervix identical with the changes in the invasive epithelium itself. From this observation there was to develop the concept that the change in the surface epithelium was the beginning carcinoma and that invasion was a later event in the disease process. In 1927 and later Schiller described these surface changes as carcinoma in a pre-invasive stage. In 1932 Broders described similar changes in various organs and stated that epithelium cannot be considered non-carcinomatous, or at the most only pre-carcinomatous, only because it is within the confines of the so-called basement membrane. Since then this theme, with reference to the cervix, has been developed by Smith and Pemberton, TeLinde, and others.

In the vaginal portion of the normal cervix the epithelium is of the stratified squamous variety. There is a gradual transition of the type of cells from the base to the surface. In the condition under discussion there is a loss of the normal stratification, the cells vary in size and shape, mitotic figures are frequent, and there is nuclear hyperchromatism. These changes are believed to be identical with those in the actually invasive epithelium of frank carcinoma. TeLinde believes that the carcinomatous changes begin in the basal layer of cells.

It must be stated that this subject is a controversial one. Furthermore, even among pathologists who believe in the concept, there will be those who will disagree in specific cases. In many instances the microscopic picture will be borderline and the diagnosis uncertain.

In 17 or more cases reported in the literature by several writers these intra-epithelial changes have been observed to precede invasive carcinoma of the cervix, and in many instances they have been found to coexist with invasive carcinoma. There is evidence that intra-epithelial carcinoma may exist for years before invasion occurs. Pund and Auerbach suggest that invasion begins about six years after the onset of the pre-invasive phase, and that there may be another six years before ulceration becomes obvious.

If these observations on the existence of a cancerous process for so long before the lesion becomes obvious are true, then our nomenclature must be changed further. One could no longer designate

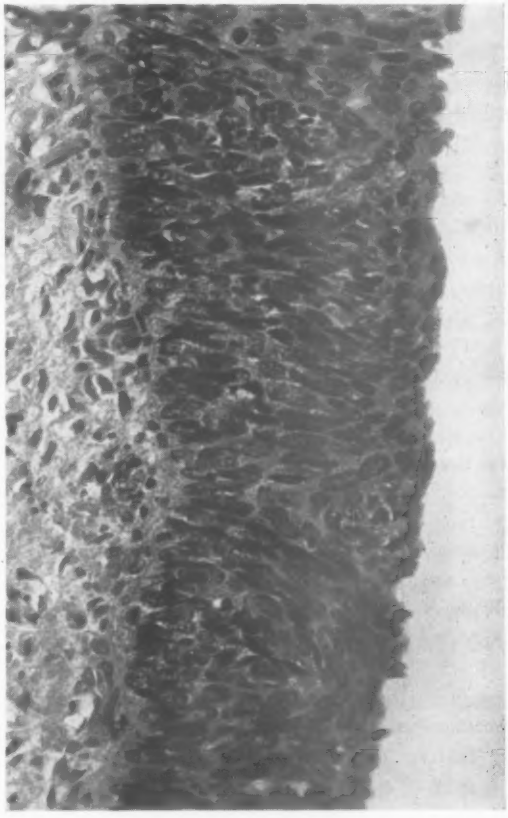

Fig. 2—S-46-3094. 400 X. Illustrative section of case of intra-epithelial carcinoma of cervix. Note loss of stratification, absence of invasion.

stage I (League of Nations) carcinoma as early. Early would be used more properly to define the clinically latent period prior to invasion and gross disease, a stage for which the designation 0 (zero) has been suggested.

If the concept of the ultimate clinical malignancy of these lesions is accepted, the early detection and treatment of them should be encouraged. As aids in the detection of early cervical carcinoma, Schiller has recommended his iodine test and Hinselmann

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has advocated the use of the colposcope. The Papanicolaou smear is a useful aid in detecting early invasive carcinoma and positive smears have been reported in carcinoma *in situ*.

As the condition may exist in grossly healthy cervices, the question arises how far we should go in biopsying these apparently healthy organs. It would be neither practical nor possible to biopsy every cervix; but when there are operations for benign disease, or when tests give suspicious findings, or when the cervix is grossly diseased, cervical tissue should be microscopically examined with the possibility of intra-epithelial carcinoma in mind.

As there are differences of opinion regarding the malignancy or potential malignancy of these lesions, and as by definition they are non-invasive at the time of diagnosis, one would expect a difference of opinion regarding their proper treatment; and their proper treatment might well be different from that of carcinoma in its invasive stage. A review of the literature and an analysis of questionnaires sent to the medical schools of the United States and Canada show that the treatment varies from simple cauterization to irradiation and radical surgery. However, the consensus is that total hysterectomy is the treatment of choice, and many advocate conservation of ovarian function in the young patients. With this treatment the cure rate should closely approach 100 per cent, but a warning should be made that this treatment is inadequate for invasive carcinoma and, therefore, associated invasion should be ruled out before it is used. Errors in diagnosis may lead to too much treatment on the one hand or too little treatment on the other.

We have observed these epithelial changes in a number of patients. In some instances it was the sole pathologic process in the cervix and in other instances it was associated with invasive carcinoma. Photomicrographs on several of the casess were projected herewith, and a series of such cases will be reported in detail elsewhere.

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BROMIDE INTOXICATION—REPORT OF TWELVE CASES*

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Today, we find that many nostrums sold across the counter as "pain killers," "headache cures," and "nerve tonics" still contain bromides. These include "B. B. Headache Powder," "Broma-Citra," "Bromo-Seltzer," "C. C. Compound," "C.C.C." or "4 C's," "E. E. Powders," "Goody's Headache Powder," "Heads-Up Headache Powder," "Neurosine," and "Miles' Nervine." Two of the much advertized "headache cures," "Standback Headache Powders" and "B. C. Headache Powders," no longer contain bromides. From such a long list, it is easy for the public to find a "headache cure" or a "pain killer" that relieves their symptoms. The psychoneurotic may find a temporary crutch and the alcoholic may find just the remedy for those symptoms produced by overindulgence, but with continued use, they end up as diagnostic problems in the hospital or in some physician's office. Then, too, there are a few physicians who do not realize the dangers of the drug and hence prescribe it loosely, or who forget to write "N.R." on the prescription. In spite of the fact that the literature contains abundant material concerning bromism, too many cases are still seen.

In 1938, Hanes and Yates[1] stated that 5 per cent of the admissions to psychiatric hospitals were due to bromism. Wagner and Bunbury[2], in a study of a thousand consecutive admissions to a mental hospital, found that 77 had bromide levels over 75 mg. per cent, and that the mental symptoms of 44 of these were due to or increased by bromides. Wuth[3], reported elevated blood bromide values in 21 per cent of a series of 238 patients admitted to the Henry Phipps Psychiatric Clinic of whom 9 per cent showed clinical evidence of bromide intoxication. Thus, it is seen that up to 9 per cent of the admissions in psychiatric institutions may be due to bromism. There are probably innumerable cases seen by physicians and tagged simply as psychotics or psychoneurotics, but many of these patients' vague symptoms may be due to a hidden bromism.

Bromides act mainly by depression of the central nervous system. With increasing blood bromide, there is a reciprocal decrease in the chloride. The bromide ion is contained only in the extracellular fluids except in the case of the red blood cells which are also permeable to chlorides. The brain cells apparently have a special affinity for bromides. However, unless the bromide is in its ionic state, it will not have any action. It is doubtful that just a fall in the chloride ion, without replacement by bromide, will produce any of those symptoms attributed to elevated blood bromide. Hiatt[4] found that when 50 per cent of the chlorides of dogs was replaced by nitrates, there was no apparent change in their behavior. It is hard to explain why some individuals develop symptoms while others do not. Millikan[5] gave sodium bromide to 36 patients over long periods in varying doses and found that all the patients who became psychotic by ingestion of the drug either had a psychoneurosis or a psychopathic personality. They were unable to produce this syndrome in any patient having a stable personality.

The evidences of intoxication[6] are produced because of the drug's action on the nervous system, glands, skin, and the gastro-intestinal tract. The early symptoms of intoxication usually are vague and may appear to be an exaggeration of those symptoms for which the drug was prescribed originally.

Early evidences of bromide action on the cortex are restlessness, weakness, headache, and loss of power of concentration. A little later emotional disturbances appear and then there may be disorientation, hallucinations, confusion, stupor, and coma. Many neurological diseases such as acute alcoholism, tabes, brain tumor, *et al.*, may be simulated. This is easily understood when one remembers that there may appear tremor of the hands and tongue, increased or diminished reflexes, a positive Babinski's sign, inability to walk, and incontinence. Any com-

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bination of these signs and symptoms may produce a most unusual picture; hence, a bizarre mental or neurological picture should merit suspicion of bromism.

The action of the bromides on the secretions of the glands is similar to that of the iodides. The secretions of the lacrimal and the mucus-secreting glands of the respiratory tract are increased and there may then appear the picture of an upper respiratory infection.

Millikan and Paul[7], in a series of 36 bromism cases, found 5 of them to have a skin rash. Detweiler[8] reported 25 per cent had skin lesions in his series. The rash usually occurs on the face and at the roots of the hair and may extend to the neck, arms, chest, and the remainder of the body. It is usually acneiform but may be nodular on the lower extremities and may resemble tertiary syphilis.

The most frequent symptoms referable to the gastrointestinal tract are: anorexia, foul breath, sordes, a thick-coated tongue, constipation, and gastric distress. The latter may be due to gastritis from the hydrobromic acid formed in the stomach.

Too much emphasis cannot be placed on mild intoxications, as these are the patients whose complaints are largely subjective. Here the patient may only complain of feeling tired, weakness, or "not my old self," and if the question concerning bromide intake is left unasked, the diagnosis will be missed.

Care should be exercised in prescribing bromides. Certainly they are useful in the physician's armamentarium, but no patient should be given a prescription for bromides unless he is seen frequently. These patients may continue to have the prescription refilled a number of times without the doctor ever realizing that this happens. There are conditions under which the drug is definitely contraindicated[9]. These are: anorexia, cerebral arteriosclerosis, congestive heart failure, renal pathology, alcoholism, psychoneurosis, dermatitis, dehydration, and tuberculosis.

In cerebral arteriosclerosis the drug will readily produce intoxication and, because in congestive heart failure, salt is restricted, it is easily seen how the blood bromide is quickly elevated. In anorexia, vomiting, and diarrhea where there is a loss of chlorides, intoxication may occur rapidly. Alcoholics may use the drug to relieve that "hang over" feeling that occurs the next day and hence have a continuance of those symptoms of which they are trying to rid themselves. Where there is kidney damage, the bromide ion which displaces the chloride ion is retained even longer. Bromides may produce an irritative reaction in tuberculosis and hence activate a dormant lesion. Some types of dermatitis and acne may be aggravated by the drug. Obviously, mental patients should not receive the drug. When bromides are used, it is most important to maintain the fluid and salt intake.

TREATMENT

Essentially, treatment consists of forcing fluids and the administration of sodium chloride to replace the bromide ion. Six to twelve grams of sodium chloride a day is sufficient to replace the bromide. More than this, if taken orally, may lead to vomiting and diarrhea. As a rule, improvement is not dramatic and it lags behind the falling bromide level. This, then, cannot be used as a guide to the clinical improvement of the patient. It has been stated[10] that with an initial level of 250 mg., a drop to 100 mg. or less may be expected within five to seven days after treatment, and nineteen days will elapse before the patients become mentally clear. Just why this delay occurs in improvement of clinical symptoms is not clearly understood. Weir and Hastings[11] have found that the ratio of bromide to chloride in the brain and the cerebro-spinal fluid is less than in extracellular serum of the rest of the body. This may be the explanation, since possibly the equilibrium between the two is reached more slowly than in other parts of the body; hence tardiness of the replacement of the bromide ion occurs in the nervous system. One other method of treatment may be tried and this is continuous Wangensteen suction.

Since the bromide ion replaces the chloride ion, and the gastric acidity in these cases is partly made up of hydrobromic acid, this reaction may be used as a method of eliminating the bromide. Moreover, Toenhort[12] treated a patient who had a bromide level of 300 mg. per cent with repeated aspirations of the gastric contents and was able to remove 5 grams with clinical recovery in six days. This would be only about 4 per cent of the total bromide content of the body, and if more could not be obtained it is difficult to explain why a patient would improve.

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CLINICAL STUDY

During a thirty-four month period from April, 1946, through January, 1949, a total of twelve cases of bromism were seen in our hospital (see Table I). There were nine men and three women. The youngest was thirty and the oldest, seventy-six years of age, the average age being fifty. The patients named physicians in six instances as their only source of bromides. One had gotten the drug from his physician and had also been taking "triple bromides" and "Bromo-Seltzer." Another had been treated by his physician with bromides and at the same time was taking "Miles' Nervine." Three patients admitted taking "Bromo-Seltzer" alone, and the source was not obtained from one patient.

TABLE I.

SUMMARY OF CASES

CASE AGE SEX	BROMIDE LEVEL MG. % WHEN DIAGNOSED	SYMPTOMS ON ADMISSION	SOURCE OF BROMIDES	ASSOCIATED DISEASES	IMPROVED
1—C.A. 48 M	200	Dermatitis, Tremor of hands	Physician	Psychoneurosis	Yes
2—M.C. 30 F	200	Nervousness, Headaches, "Crying Spells," Antagonistic, Personality Changes	Physician	None	Yes
3—O.L. 52 M	300	Weakness, Nervousness, Worried, Motor activity diminished, Tongue coated	Physician and Triple Bromides Bromo Seltzer	Alcoholic	Yes
4—D.H. 52 M	250	Irrational, Headaches, Chills, Semi-comatose, Dehydrated, Coated tongue, Incontinent, Rales in lung bases	Physician	Alcoholic	Yes
5—B.G. 59 F	300	Confused, "Pains all over my body," Nervousness, Weakness	Bromo Seltzer	None	Treated by L.M.D. at home. Improved.
6—W.S. 51 M	300	Weakness, Dyspnea, Anorexia, Weight loss, Disoriented	Bromo Seltzer	Alcoholic	Yes
7—E.B. 37 M	250	"Felt tired," "Aching all over"	Bromo Seltzer	Psychopathic Personality	Yes
8—J.G. 54 M	75	Dizziness, Occipital pain, Insomnia, Nervousness, Lips slightly cyanotic, Fine rotary movements of both eyes associated with sudden changes in posture	Physician	Alcoholic, Cerebral Arterio-sclerosis	Left hospital. Treated by L. M.D. No follow-up.
9—C.L. 30 M	100	Anorexia, Weight loss, Nervousness, Insomnia, Epigastric distress, "Smothering Spells"	Physician	None	Yes
10—I.K. 76 M	190	"It's all over me," Dizziness, Anxiety	Unknown	Hypertensive Arteriosclerotic Cardiovascular Disease, Cerebral Arteriosclerosis	Yes
11—E.F. 70 F	100	Confused, Nervous, "Unable to be alone," Pneumonia	Physician	Generalized Arteriosclerosis Congestive failure	Yes
12—A.R. 47 M	300	Headaches, Irrational, Tongue Thickly Coated, Pupils pinpoint, Reflexes hyperative	Physician Miles' Nervine	Alcoholic	Died

It was interesting to see the associated diseases which these people had besides bromide intoxication. Four were alcoholics; and there was another alcoholic who also had cerebral arteriosclerosis; one of the four had congestive failure. One had a psy-

chopathic personality, and one was a psychoneurotic. These are the people who should not take the drug, or at least should have been under proper supervision while using it. Associated diseases were not present in three patients.

The blood bromide levels ranged from 75 to 300 mg. per cent. Case 8 (see Table I) was included in this series in spite of his level being only 75 mg. per cent because his symptoms of dizziness, occipital pain, insomnia, and nervousness could have been due to bromism. This is more apt to be true with such a low level when cerebral arteriosclerosis, which this patient had, is present. Unfortunately, he was not treated here in the hospital and there was no follow-up report from the physician who treated the patient.

As can be seen from Table I, many of the symptoms were vague. These included weakness, nervousness, insomnia, dizziness, headache, and anorexia which are hardly specific of any disease. Others had reacted to the drug to the extent that when seen they were irrational or semi-comatose.

Ten patients improved with treatment, one died, and the subsequent course of one (Case 8) is not known.

CASE REPORTS

Five of the twelve cases are presented in more detail because of various points which they illustrate.

Case I.—C. A., a 48 year old man, was admitted to the hospital on December 13, 1948, complaining of "skin trouble." He stated that he had had psoriasis around his elbows for several years. One month before admission, he noted a small papule over his left tibia. He scratched this lesion, and shortly thereafter the skin over the lower tibia became inflamed and oozed a clear serum. Several days before admission, a papular red rash appeared on his face and lower extremities. This had been treated with "Congo Red" and a "sulfa" ointment without any relief of his symptoms. The patient was of low intelligence and several days later, after repeated questioning, he admitted having taken "white capsules with a blue band" which had been prescribed by his local physician.

Physical examination revealed a man continually scratching himself who answered questions slowly and with hesitancy. There was a coarse tremor of his hands. The lesions involving the entire face were erythematous papules. There were areas varying in size from 1 to 5 cms. in diameter over the elbows, lower extremities, and back. They were red and covered with white scales. The skin over the lower two-thirds of the left tibia was acutely inflamed and "weeping." The remainder of the physical examination was essentially negative.

Laboratory findings: The hemoglobin was 78 per cent and the leukocyte count 11,350, with 48 neutrophil segmenteds, 2 neutrophil stabs, 38 lymphocytes, 3 monocytes, 7 eosinophils, and 2 myelocytes. The Kline was negative and urinalysis was normal. Spinal tap was negative. The blood bromide level was 200 mg. per cent.

Course: The patient was given 8 grams of sodium chloride daily and fluids were forced. 50 mg. of "pyribenzamine" were given four times a day for itching, and normal saline dressings were applied to the exudative lesions of the left lower extremity. On December 20, seven days after admission, the bromide level was 100. Three days later it was 75. The patient was discharged 17 days after admission at which time the skin lesions had cleared but he continued to have "nervousness." He was readmitted to the hospital on January 25, 1949, because of itching and oozing of the skin over the upper and lower extremities and face. Physical examination revealed an extensive, "weeping" rash of the face, thighs, scrotum, and the flexor surfaces of the upper and lower extremities. At this time, he had a coarse tremor of his hands. The tongue was red and the angles of the mouth were fissured. The bromide level was 75 at this time but he denied having taken any further medications since the previous admission. He received 12 grams of sodium chloride daily, the skin rash was treated with calamine lotion and oat meal baths, and he was given "pyribenzamine," 50 mg. every four hours. The rash did not improve and on February 1, "pyribenzamine" cream was used topically. Following this there was a marked clearing of the skin and on February 12, the bromide level was less than 75. The patient was discharged the next day at which time his skin was clear. While in the hospital during this admission, he had numerous vague complaints which did not improve with therapy and his behavior was that of a confirmed psychoneurotic.

Many physicians have the misconceived idea that they should consider bromide intoxication only in

those who have a dermatitis. In our series of twelve cases, this patient was the only one who had a dermatitis. In all probability this was not a primary dermatitis, but an atopic one which had simply been aggravated by bromides.

Case II.—This 30 year old white female, M. C., was admitted to the hospital on January 17, 1949. It was difficult to obtain a history but apparently she had been "nervous" for a number of years and had been taking various medications because of this. She also had a history of severe frontal headaches, and her husband stated that she had been emotionally upset prior to admission and "cried all of the time."

Physical examination revealed an uncooperative female who became angrier as each additional question was asked by the examining physician. The skin and mucous membranes appeared slightly cyanotic. The remainder of the examination was negative.

Laboratory findings: The hemoglobin was 70 per cent, red blood count 3.4 million, total leukocyte count was 6,600 with a normal differential. The urine showed a few pus cells in the sediment but otherwise was not abnormal. The Kline reaction was negative. The blood bromides were elevated to 200 mg. per cent.

Course: She was treated with sodium chloride, grams 3 four times a day, and given intravenous fluids. Six days after admission her personality changed completely and by discharge she had become very cooperative but continued to be "nervous." She was discharged on sodium chloride, grams 3 three times a day, and phenobarbital. Follow-up examination on February 2, 1949, found her much improved but still complaining of headache, and at this time she was advised to discontinue the sodium chloride. On February 15, patient's bromide level was less than 75 mg.

This patient was probably given bromides by her physician who did not think that she would continue taking the drug, or did not realize its toxicity. Here with treatment and the discontinuance of the drug, a complete reversion to a normal personality was seen to occur within a few days.

Case IV—D. H., a 52 year old man, was admitted in a semi-comatose condition on July 7, 1948, and the history was obtained from his wife. She stated that he had consumed large quantities of alcohol for a number of years. Two months prior to admission he developed nausea, vomiting, and abdominal pain and was hospitalized at another hospital. He was irrational during most of his stay there and after one month was discharged. Since that time, he had continued to be irrational at intervals. He also had had frequent headaches, and three days before admission to our hospital had had a severe headache and a definite chill.

Physical examination: The patient was malnourished and semi-comatose. The temperature was 99.8 degrees F. The skin and mucous membranes were very dry. Examination of the fundi revealed the discs to be hyperemic with definite haziness of both nasal borders. The left ear drum was hyperemic and retracted. The tongue was coated. Crackling rales were heard in both lung bases. The patient was also incontinent.

Laboratory findings: Two days after admission the hemoglobin was 80 per cent, red count 3.99 million, and total white count 6,950 with a normal differential. The urinalysis showed one plus albumin, four plus sugar, 25-30 red blood cells, and 15-20 pus cells. (This was after a retention catheter had been inserted and the patient had received intravenous glucose.) The blood urea-nitrogen was 11 mg. per cent. Examination of the spinal fluid revealed it to be clear and the pressure was normal. The globulin was increased but the microscopic examination was negative. X-ray of the skull was negative, and x-ray of the chest showed a moderate amount of infiltration of the perihilar regions.

Course: On admission the impressions were (1) meningitis, (2) cervical spine lesion, (3) cerebral neoplasm, (4) diabetes mellitus, and (5) delirium tremens. The patient was started on intravenous fluid containing vitamins B and C and penicillin every three hours. On July 13, the possibility of bromism was discussed and a bromide determination at this time revealed the level to be 250 mg. He was given 2 enteric-coated sodium chloride tablets four times a day and fluids were forced. By July 16, he was still irrational although he had begun to take food by mouth at times. On the 19th, the patient was able to sit in a chair and walked with difficulty. His sensorium had begun to clear at this time. On July 20, the bromide level was 175 mg. per cent, and by July 22 he was very cooperative and was able to dress himself. At this time he knew his age, home

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address, and former occupation. By the 24th, he was rational and the bromide level was 100 mg. He was discharged 21 days after admission at which time he seemed well oriented, but his speech was somewhat hesitant and he had some difficulty in remembering past events. He was last seen one month after discharge when he appeared to be in good health. His bromide level was less than 75 mg. at that time, and his urinalysis was normal.

This case illustrates the difficulty in making a diagnosis. The patient had been in another hospital for one month and had not been diagnosed. When seen in our hospital, it was a week before a diagnosis of bromism was considered because of the similarity of the signs to those that might be found in delirium tremens, meningitis, and brain tumor. This man was a known alcoholic, and it was later learned that his physician had been treating him with bromides. Unfortunately, he had continued taking the drug for some time, ending up in the hospital.

Case V.—This 59 year old white female, B. G., was admitted to the hospital on March 30 and discharged on April 10, 1947. Her history was difficult to obtain as she was confused on admission. She stated that she had had "pains all over my body" and generalized weakness for several months. She had always been nervous, but had become increasingly so during the six months prior to admission. During her hospitalization, it developed that she had been taking large quantities of "Bromo-Seltzer."

Physical examination revealed an apathetic, confused, white female who complained of inability to move except with the greatest effort because of weakness. The strength in her hands was fairly good and she was able to flex and extend her knees and ankles. On pelvic examination, the perineum was markedly lacerated and the rectal sphincter was badly torn in the anterior portion. The remainder of the physical examination was essentially negative.

Laboratory studies showed the hemoglobin to be 90 per cent, and the white count was 5,800 with a normal differential. The Kline reaction was negative and urinalysis was normal. Electrocardiogram was within normal limits.

Course: This patient was confused at times during her hospitalization and was very difficult to control. There were times when she talked continuously and incoherently. Blood was drawn a few days after admission and sent to another laboratory for bromide analysis. The report was received the day before the patient was discharged and was 300 mg. The patient left the hospital, and the family physician was advised to administer sodium chloride and to force fluids. The patient was never seen again by us after she left the hospital.

A report from her family physician one month later indicated that her sensorium had cleared considerably, and she had become cooperative. No further bromide level was obtained. Here is a case which would probably have been labeled "psychoneurotic." She may have been taking the drug for similar complaints; but as her physician stated, she had improved with treatment.

Case XII.—A. R., a 47 year old male, was admitted to the hospital on December 23, 1948. At this time, he was irrational and uncooperative. The history was obtained from his wife. She stated that he had been a "heavy drinker" for years, had been "nervous" for some time, and had been taking medications prescribed by his local physician. Several weeks prior to admission, he had taken two bottles of "Miles' Nervine" to his wife's knowledge. He returned from work two weeks before admission at which time he complained of headache. At that time, he became confused and irrational and was seen by his local physician who treated him at home with "bromides" for one week. During that time, he complained of headache on various occasions. At the end of that time, he was taken to a local hospital. According to a communication received after the patient's death, the doctors at the local hospital thought that the patient had a brain tumor, abscess, cerebral hemorrhage, or encephalitis. For five days he received penicillin and intravenous fluids without improvement. After this, he was sent to our hospital.

Physical examination revealed a well-developed and well-nourished male lying in bed; semi-stuporous, disoriented, cooperative but slow to respond. The tongue was thickly coated, the pupils were pinpoint, and the reflexes were hyperactive. Otherwise, the remainder of the physical examination was essentially negative.

Laboratory findings: On December 24, the day following admission, the hemoglobin was 84 per cent, the leukocyte count 10,250, with a normal differential. The Kline reaction was negative and the urinalysis was normal. The blood bromide was reported as being more than 300 mg. per cent on the day of

admission. Spinal fluid examination done at the other hospital was normal.

Course: The patient had to be restrained on admission and received sodium luminal for restlessness. Fluids were forced by mouth and he received 5 per cent glucose in normal saline intravenously twice a day. However, because of his irrational condition, he required large and frequent doses of sedatives ("nembutal," paraldehyde, and sodium pentothal). On admission, his temperature was 98 degrees F. (axillary). However, the next day it was 101.6 degrees F. and was intermittent to this level for three days. It became impossible to continue intravenous fluids because of the patient's condition, and a nasal tube was passed on December 27, 1948. He then received a diet consisting of carbohydrates 300 grams, proteins 100 grams, and fats 50 grams, for each 24 hours, divided into six feedings. In addition, he received two grams of sodium chloride at each feeding and 2,000 cc. of water was added to the diet. He also received vitamins B and C intramuscularly. That night he began to have diarrhea and was given paregoric and "Kaopectate" after each loose stool. Fluids were continued and the next day he was put on sulfadiazine and penicillin. His temperature began to rise higher than 102 degrees the night the diarrhea commenced. By the next afternoon, it reached 106 degrees rectally and the patient died. Autopsy was performed but did not contribute any further information as to the cause of death.

There have been only a few cases reported in the literature of death due to bromides. Bunbury and Wagner[13] reported two cases due to indiscriminate use of bromides. Barbour[14] has also reported one death.

This death was probably due to bromism, or at least it contributed heavily to the cause of death. Since he had been in such a poor condition for some time, it may have been that the diarrhea was all that was needed to tip the scales against him.

Summary

Twelve cases of bromide intoxication, including one fatality, are reported in order to re-emphasize the danger of the use of bromides without adequate control.

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CUSHING'S SYNDROME: REPORT OF TWO CASES

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Cushing in 1932 reported twelve cases, all in young adults which revealed the following symptomatology:[1]

1. Rapidly acquired, usually painful adiposity of the face, neck, and trunk.
2. Tendency to kyphosis from an "unusual softening of the bones of the spine."
3. Sexual dystrophy, early amenorrhea in females and ultimate impotence in males.
4. Hypertrichosis of face and trunk in females and preadolescent males, and possibly the reverse in adult males.
5. Dusky, plethoric appearance of the skin and purplish striae.
6. Hypertension with a blood pressure ranging from 178/100 to 230/170.
7. Tendency to polycythemia.
8. Variable backaches, abdominal pains, fatigability and weakness.

Other features noted were acrocyanosis, ecchymosis, aching pains in the eyes, slight exophthalmus, dry skin, polyphagia, polydipsia, polyuria, edema of the lower extermities, and susceptibility to infection.

This syndrome, which now bears Cushing's name, he thought was due to the presence of a basophilic adenoma of the pituitary gland. He suggested that the over-production of gonadotropic hormone by the basophile cells might be responsible for the pathology analogous to over-production of growth hormone by the acidophile cells in acromegaly. Cushing pleaded for more pathologically verified cases, and less clinical speculation as to the etiology of the condition. Similar cases have accumulated in the literature and pathological studies have been instructive. These studies have revealed instances of basophilic adenoma, with or without adrenal adenomas. In a number of cases malignant tumors of the adrenal gland were found. In one instance an adenoma apparently arising from the pars intermedia of the hypophysis was revealed.[2] Arrhenoblastoma of the ovary[3] has also been reported as a causative factor. The English pathologist Crooke[4] reported twelve cases of Cushing's disease, in six of which pituitary adenomas occurred. In three cases there was neoplasm or hyperplasia of the adrenal cortex without pituitary adenoma. The remaining three likewise failed to show pituitary adenoma but showed neoplasm of the thymus gland as the presumed pathological basis. In addition, Crooke reported after a careful study of the pituitary glands of the twelve cases an abnormality common to all, namely a hyaline change in the basophile cells of the anterior pituitary, which was not observed in a study of 350 pituitary glands from other conditions. This he believed to be of considerable significance.

Obviously, then, the evidence at hand suggests that this syndrome is not a response to one specific type of lesion. The pathologic physiology of the disease is obscure. The behavior of the gonads is not that ordinarily associated with over-production of gonadotropic hormone. The frequent occurrence of bilateral adrenal cortical hyperplasia in basophilism does, however, suggest over-production of the cortical hormones. Certainly there is strong support for the view that the problem is in the nature of hyperadrenocorticism, whether initiated in the hypophysis or adrenals.

Evidence at hand would indicate that the adrenal cortex elaborates numerous hormones. The total number of such hormones isolated is reported to be in excess of twenty-five. Chemically, the active hormones are identified as steroids. Studies with adrenalectomized animals have confirmed biological activity of a number of these steroids, variously stated to be from six to ten.

A classification of the steroid hormones on the basis of biological activity, which corresponds with the accepted concepts of clinical activity of the adrenal cortex, has been offered.[5] Accordingly, the first group of compounds are those which regulate water and electrolyte metabolism. This is particularly significant in Addison's disease where sodium excretion, potassium retention and changes in extracellular fluids are so striking. The best example of a steroid affecting this type of metabolic disturbance is desoxycorticosterone. A second group of compounds which influence carbohydrate and protein metabolism are well recognized. The injection of

such hormones results in an increased blood sugar and liver glycogen content. This response appears to follow an acceleration of protein catabolism. Following deamination of protein, the amino acids thereby derived, may be converted into glucose. Another factor appears to be that of an inhibitory effect of the steroid upon oxidation of glucose in the tissues. Structually this group of steroids all have an oxygen atom on C 11 and are known as corticosterones. Urinary assays for these corticosterones or corticoids most likely do not indicate the quantities of the substance formed in the gland. However, varying levels of urinary corticoids probably reflect changes in the activity of the cortex. Finally, there is the third group of compounds which exhibit the properties of the sex hormones. These are the well known androgens, estrogens, and progesterone. There are also demonstrable in the urine a group of steroids which have a ketone group on the seventeenth carbon atom and a free methylene group. To these have been applied the name 17-ketosteroids. Androgenic properties are possessed by some of the 17-ketosteroids. In the male urine two-thirds of the 17-ketosteroids are believed to be derived from the adrenals, while the testes are the source of the remaining one-third. In the female urine the total content of the 17-ketosteroids is believed to be derived from the adrenal gland. Differentiation of 17-ketosteroids into Alpha and Beta fractions has been accomplished. Elevation of the Beta 17-ketosteroids has been found in carcinoma of the adrenal cortex. The exact source of the 17-ketosteroids in the adrenal is not proven; however, it is likely concerned with androgenic function and has an anabolic effect on protein metabolism.

Alteration in the amounts of the steroids secreted by the adrenal cortex, particularly in hyperfunction where there is an excessive production, seems to result in fairly typical clinical syndromes. Pathologically the chief findings in the cortex are hyperplasia which may be localized or diffuse, adenoma usually weighing from two to four ounces which exhibit a predisposition to malignant changes, and carcinoma. The carcinoma metastasize most frequently to the lungs, liver, and brain.

The adrenogenital syndrome results when there is a hypersecretion of diverse cortical steroids which are androgenic in function. The changes observed are those of masculinization. It is approximately five times more frequent in the female, and may originate in fetal life, infancy, childhood, or adult life. Intravenous pyelography or perirenal air insufflation may reveal the presence of an adrenal tumor. Urinary 17-ketosteroids are markedly increased as an expression of this increased androgenic activity.

The classic studies of Albright[6-7] indicate that another type of adrenal cortical hyperfunction is responsible for the changes observed in Cushing's syndrome. These investigators believe that there appears at puberty simultaneously with the onset of estrin in the female, and probably at the time of the onset of testosterone in the male, a steroid cortical hormone which is somatotrophic in effect, controls pubic and axillary hair, and excretion of 17-ketosteroids in the female. This he has called the nitrogen or N hormone, and its function is to stimulate anabolism. Its presence in the body extends well into the later years of life, considerably beyond the menopause in the female and to a corresponding period in the male.

At the same time there is present in the body another adrenal cortical steroid hormone which in contrast to the above inhibits anabolism. It furthermore breaks down lymphoid tissue, releasing immune globulin which inhibits hexokinase and interferes with the oxidation of sugar. This results in increased deposition of glycogen in the liver. This steroid is under the control of the adrenocorticotrophic hormone of the pituitary gland. Its structure reveals an oxygen on the eleventh carbon atom. The "11 oxycorticosteroids" determination is a quantitative measure of its presence. This hormone has been designated the adrenal cortical sugar or "S" hormone by Albright. In health these opposing "N" and "S" hormones exist in normal amounts. Excessive production of the "S" hormone in the young adult produces Cushing's syndrome. Urinary assays reveal a marked increase in the urinary corticoids. There is also an increase in the 17-ketosteroids which is described as compensatory on the part of the "N" hormone in the presence of excessive quantities of "S" hormone. Thus, it would appear that hyperfunction of the cortex with hypersecretion of androgenic substances and or "N" hormones results in the adrenogenital syndrome; whereas hyperfunction of the adrenal cortex with hypersecretion of hormones which inhibit anabolism, the corticosterones or the sugar or "S" hormone produces the clinical picture of Cushing's syndrome. Albright believes that careful pathological studies will in most instances reveal the

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hyaline degeneration of the basophile cells of the pituitary gland described by Crooke. It is also interesting that in the later years of life after there has been a cessation of the sex hormones, particularly estrogen, and a decrease in the somatotrophic or "N" hormone, the unopposed action of the "S" hormone which by its inhibition of anabolism is responsible for the production of osteoporosis.

The following is a report of two cases of Cushing's syndrome.

Case I: Mrs. A. G. is a 43 year old married woman. There have been no pregnancies. The patient presented herself with chief complaint of puffiness, bloated feeling, and splotchiness.

Present Illness: Prior to November, 1945, this patient had been in excellent health, very active, energetic, and her personality was distinctly that of an extrovert. Her last normally scheduled period was in October 1945. Then five weeks later, November 17, 1945, she had her last period which was not entirely normal but not greatly abnormal. Since this time there has been no evidence of menstruation. Some two weeks after the last period she began to feel quite nervous inside and became aware of suddenly getting fat, particularly in the chest and abdomen. She comments that the abdomen became so fat that it would tremble. This was next followed by the feeling of puffiness which she states that she could definitely see. At one time the puffiness would be in the epigastrium, and at another time she would be aware of it in the chest and on occasions she has felt that her knees were puffy. When she becomes nervous she is aware of purplish mottled type of splotchiness over the body. Likewise she has experienced hot flashes following which she perspires a great deal and then gets icy cold. Since all of this has happened she has observed a marked tendency to bruise very easily, something which she had never noticed before. In a recent examination pressure of the stethoscope and the application of the tourniquet both left purplish bruised areas.

All of her life she was known to have a normal blood pressure and early in the fall of 1945 her blood pressure was low. However, during an examination in the last few days her blood pressure was found to be 250/168. She was put on a rice diet and there followed a drop of 25 points in the blood pressure, and at the same time she lost three pounds in weight. However, prior to the institution of the rice diet, from the onset of her illness in November she gained fifteen pounds in weight.

She has always known that her eyes were somewhat prominent but of late the prominence has become quite marked until they protrude and associated with this is a marked watering of the eyes.

Her general nervousness and trembling is quite disturbing. Whenever she attempts to do anything the trembling is quite marked. However, if she remains at home quietly she feels much more relaxed and the trembling is decidedly reduced.

The physician who has just examined her feels that she probably has Cushing's syndrome and she was referred to verify his opinion.

Family history is unessential except that one sister was large and was told that she had gland trouble, the exact nature of which is not known.

Physical examination reveals the patient to be 5′ 3¾″; weight 153½ lbs.; temperature 98.4.

The patient appears to be quite obese. This obesity is strikingly confined to the chest, abdomen, and neck. The extremities however do reveal some obesity proximally but the legs and forearms are of normal size or possibly somewhat small. The skin, particularly of the legs and thighs, reveals a purplish mottling. There are also numerous scattered bruises over each leg. There is increased facial trichosis which also involves the upper lip and the neck. Likewise there is trichosis in the midline of the abdomen extending up from the pubic hair. There are a few purplish striae of the lateral abdominal wall on each side; under each breast there are purpuric spots, and over the right arm there are numerous purpuric spots at the site of the pressure from the blood pressure cuff applied a few days ago. The eyes are distinctly exophthalmic. The pupils are equal and react to light and accommodation. There is slight lid lag. The fundi were essentially normal. The pharynx is injected and the tonsils are small and adherent. The teeth all appeared to be vital. There was a definite tremor of the tongue. There was no lymphadenopathy. No thyroid abnormality was detected. The chest was symmetrical, short, thick, with a wide costal angle. The lungs were clear to percussion and auscultation. Heart: Cardiac dullness extended to a point approximately 10 cm. from the mid-sternal line in the left fifth interspace. Retro-manubrial dullness was not increased. Heart sounds were of good quality without undue accen-

tuation of either second sound. There were no murmurs. Action was entirely regular. Peripheral vessel walls were not palpable. The pulse rate was 89 to the minute. Blood pressure—right arm 190/120; left arm 190/130. The abdomen was definitely protuberant with thick walls which were relaxed. The liver border was palpable about 2 finger-breadths below the costal margin on deep breathing; otherwise, no tenderness, masses, nor rigidity were detected. The spleen could not be felt. The spine was straight without tenderness or limitation. The joints of the upper and lower extremities were freely movable without evident abnormality. There were a moderate number of varicosities of the legs, more marked on the left. The reflexes were all active and equal. Pelvic examination revealed no abnormality. Laboratory studies had been done prior to the patient's reporting to me and were not repeated. They were as follows: hemoglobin 110%; sedimentation rate 4 mm. in one hour. Wassermann was negative. Non protein nitrogen 40 mgms. Urinalysis revealed a trace of albumin and a rare RBC was reported. Basal metabolic rate was minus 14%. Electrocardiogram revealed a somewhat low T wave in Lead II and inverted T wave in Lead III, with left axis deviation.

In view of the patient's amenorrhoea, rather suddenly developing obesity of the trunk (or buffalo type) which was somewhat uncomfortable, definite purpura, hypertension, hypertrichosis, exophthalmus, and, though the red blood count was not done, with the hemoglobin of 110% certainly suggesting the possibility of polycythemia, it was felt that Cushing's syndrome was a very likely possibility.

The patient entered a medical center in another city. Here the findings revealed a downward displacement of the right kidney shadow on intravenous and retrograde pyelography. On peri-renal air insufflation a mass the size of a baseball was revealed superimposed upon the upper pole of the right kidney. 17-ketosteroids were reported as 18.11 mgms. in a twenty-four hour specimen of urine and represents moderate elevation. The patient was operated on and a round tumor the size of a baseball, weighing 247 grams, was removed. The pathological diagnosis was adenocarcinoma of the adrenal cortex.

Post-operatively the patient responded remarkably well, became symptom free, the 17-ketosteroids dropped to 7.98 mgms. per twenty-four hours when she was discharged. Approximately one year later the patient appeared to be in complete remission. The blood pressure averaged 130/85. An x-ray examination of the chest, however, revealed areas of increased density compatible with pulmonary metastases, and the 17-ketosteroids had risen to 12.5 mgm. for twenty-four hours.

Case II: Mrs. J. L. K., age 37, married. Seen November 13, 1947.

Chief Complaint: Swelling of the face; nervousness for two years; watery blisters on the eyes.

Present Illness: Patient dates the onset of her present illness to approximately two years ago. At this time she reports that she would wake in the morning and observe that there was a swelling and flushing of the forehead, face, and the scalp, accompanied by increased lacrimation of the eyes. Also there would appear on the white part of the eyes what looked like small water blisters. These symptoms would persist for a good part of the day but would gradually disappear as the day progressed. She thought that whenever she would rest the symptoms would promptly disappear. With the swelling there has been no itching but at times she would experience a burning and tingling. With the onset of these symptoms she has become quite nervous and she has also observed that the swelling is gradually increasing until now it involves her face and neck as well, and it is more constant. Likewise, she has observed that she seems to be getting fuller in her trunk while her arms and legs are spared. There is likewise some increase in the prominence of her eyes. She has been impressed by an increased tendency to bruise and now the slightest blow will leave large purple spots over her body. She has always had irregular menstrual periods. During this time they have decreased in frequency and in this year there have been only two periods, one in June and one in August. In all of this time she has gradually felt worse. She has worried a great deal about the fullness and her general appearance. She has seen many doctors and the diagnosis has been invariably either the menopause or an allergy. Her father was an asthmatic and she occasionally has a little wheezing. She was studied from an allergic point of view but no conclusions were reached. Subsequently she was studied at another clinic and after exhaustive studies, including a very strict elimination diet, she felt no better. On many occasions she

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has taken hormones and it is her belief that they have given her the only relief she has had.

Family history is unessential. Patient has had no serious illness other than jaundice in 1932 or '33.

General physical examination revealed her height to be 4′ 9¾″; weight 110; temperature 97.6. The patient does not give the impression of being obese. However, the head, neck, and trunk do seem to be somewhat out of proportion. The extremities are small. The skin generally was dry with moist palms. There was a distinct flushing of the face and neck. There were numerous superficial dilated capillaries across each cheek and the bridge of the nose. The eyes were distinctly prominent with slight puffiness of the upper lids. There was increased lacrimation and at the lateral margin of the right sclera there was what appeared to be a very small bleb. There was some slight facial hypertrichosis and a mild hypertrichosis of the trunk, particularly of the back. The eyes reacted normally and the fundi were within normal limits. The ears, nose, and throat were negative. The teeth all appeared to be vital. There was no lymphadenopathy. The thyroid appeared to be normal. The chest was symmetrical. The lungs revealed an occasional sibilant rale. The heart was not enlarged. There was a systolic blow over the pulmonic area. The rate was 86. Vessel walls were not thickened. Blood pressure right arm was 168/100; left arm 164/100; popliteal pressure 210/140. The tourniquet test was within normal limits. No abnormalities were detected in the abdomen. The joints were entirely normal, freely movable. Pelvic examination failed to reveal any abnormality. Laboratory studies revealed hemoglobin 101%; red blood count 5,240,000; white blood count 15,000; with 76% polys. Blood platelets were normal. The sedimentation rate was 2 mm. in one hour. The urine revealed a specific gravity of 1.010; there was a trace of albumin; otherwise, the urine was negative. The stool was negative for occult blood. The Wassermann reaction was negative. The glucose tolerance test revealed fasting blood sugar 87 mgms.; after one hour 224 mgms.; after two hours 156 mgms. Intravenous pyelogram was normal. There was nothing to indicate any pressure on the kidney from the adrenal gland. X-ray of the skull showed the sella turcica to be of normal size and contour. The bones of the skull appeared to be normal, also those of the lumbar spine and the pelvis. On X-ray the liver shadow appeared to be somewhat enlarged.

This patient also revealed a tendency toward obesity of the trunk with normal extremities, hypertension, slight hypertrichosis, exophthalmus, suggestive tendency to polycythemia, and a disturbed glucose tolerance which was definitely of the diabetic type. These symptoms strongly suggested the possibility of an endocrine problem and the idea of Cushing's syndrome was entertained. She was admitted to a nearby medical center for study.

A very comprehensive work-up which in general substantiated our preliminary studies was done. Complete blood chemistry studies were done and were normal. Of interest for this discussion is the study of the urinary 17-ketosteroids which were reported as 32.64 mgms. for twenty-four hours. This represents a distinct increase. The normal range of 17-ketosteroids is from 4 to 14 mgms. per twenty-four hours. Study of the urinary gonadotropins revealed an activity of less than two rat uterine units per twenty-four hours and are against any hyperactivity of the pituitary. The elevated 17-ketosteroids, however, are in line with a diagnosis of Cushing's disease. The normal range for Beta ketosteroids was given as 0.1 to 1.9 mgms. per twenty-four hours, and a value of 6.2 mgms. reported in this patient represents a significant increase. It is the impression of some workers that this finding is indicative of carcinoma of the adrenal cortex. An exploratory laparotomy was advised. The patient was operated on on the 13th of April, 1948. The left adrenal appeared to be normal. The right adrenal gland revealed a large vascular tumor about three inches in diameter. This tumor was enucleated and apparently totally removed. The patient had a rather stormy convalescence post-operatively but finally rallied and appeared to be doing nicely when she died suddenly. No cause for death could be demonstrated at autopsy. Pathological report on the adrenal tumor revealed a carcinoma (adenoma malignum).

SUMMARY

Originally Cushing's syndrome was believed to be due to a basophilic adenoma of the pituitary gland. Subsequent case reports and investigations have demonstrated involvement of the adrenal cortex by hyperplasia, adenoma, or carcinoma. Whether of pituitary or adrenal cortical primacy, this clinical picture is so striking, the designation Cushing's syn-

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drome appears justified in each instance.

Recent studies indicate that Cushing's syndrome is produced by hyperfunction of the adrenal cortex with excessive secretion of that hormone with an oxygen on the eleventh carbon atom, 11-oxycorticosteroid. This steroid inhibits anabolism with disturbance of protein and sugar metabolism. Urinary corticoids are markedly elevated and there is a compensatory elevation of 17-ketosteroids. Careful pathological studies, it is believed, will in most instances reveal hyaline changes in the basophil cells of the pituitary gland.

Two cases of Cushing's syndrome are presented. In each instance an adrenal cortical tumor was found at operation which pathological examination revealed to be carcinoma.

One patient experienced a complete remission of symptoms but subsequently developed pulmonary metastasis. The second patient died suddenly of unexplained cause post-operatively.

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1100 Church Street.

Find Blood Test for Cancer Not Suitable for Diagnosis at Present.

The Huggins-Miller-Jensen blood test for cancer does not appear suitable at present as a diagnostic test, in the opinion of two researchers from the Department of Experimental Pathology, Quincy (Mass.) City Hospital. The test, based on albumin disturbance in cancer patients, was first reported about a year ago by Dr. Charles B. Huggins of the University of Chicago.

The diagnostic value of the procedure followed by Dr. Huggins and his co-workers was tested by Dr. Otakar J. Pollak and Adeline Leonard, B.S. Their report on test results from blood serums from 80 patients with proved malignant growth and on control serums from 170 patients appears in the March 25, J.A.M.A.

In seven of the 80 patients with proved malignant growth, the test failed to indicate the presence of cancer. In 23 of the 170 persons in whom malignant growth was excluded on the basis of clinical signs and laboratory and x-ray study, the test indicated malignancy. The total number of false reactions in the series of 250 persons was 30 (12 per cent).

"At the present time, this reaction is not suitable as a diagnostic test," the researchers point out. "Further investigation might bring about the development of a reaction the result of which would show better correlation with disease."

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CLINICOPATHOLOGICAL REPORTS

From the Case Records of the Medical College of Virginia and the University of Virginia Hospitals.

HARRY WALKER, M.D., *Editor*
WILLIAM KAY, M.D., *Associate Editor*

CASE NO.: B-63005

This 62 year old, white, unmarried female entered the hospital in a confused state. According to the family the patient had been markedly depressed since the death of her mother two years previously. Her depression was marked and during the past few weeks had become even more severe. For the past two weeks the patient had stated that upon awakening she was confused both in the morning and following her afternoon nap. This confused state cleared in approximately an hour. Ten days before admission the patient had a severe dizzy spell upon awakening; however, she did not faint or fall. The night of admission the patient was feeling well and was preparing to take a trip. Just prior to leaving, she collapsed while in the bathroom. She was seen shortly thereafter by the ambulance physician, who described her as being quite confused, cold, and covered with perspiration. The blood pressure was 100/60. The confusion cleared somewhat upon being brought to the Emergency Room and the blood pressure returned to 120/85. The patient had been taking questionable amounts of bromides for her nervousness and depression for an unknown length of time.

Physical Examination: Pulse 88, respirations 18, blood pressure 120/85, temperature 98.6° orally. The patient appeared to be a fairly well developed, thin, elderly, white female in a partially confused state and extremely hard of hearing. Examination: skin normal; lymph nodes not enlarged; pupils reacted to light and accommodation. There was a left sub-conjunctival hemorrhage and periorbital contusion. Fundoscopic revealed grade III arteriosclerosis, hard exudates, A-V nicking, narrowed vessels, occasional punctate hemorrhages. There was a hematoma of the left lid. The nose was normal. Mouth and pharynx were normal. The protruded tongue was in the midline. The neck was supple, no stiffness, trachea was in the midline, no venous distention. Respiratory movements were symmetrical. Lungs were clear to auscultation and percussion. Heart: Apex beat was in the 6th intercostal space, 1 cm. beyond the midclavicular line. There was a soft apical systolic murmur, no thrills noted. The rate was 88, the rhythm was regular. Abdomen: Poor relaxation. Liver was palpated 2-4 cm. below the costal margin. The kidney and spleen were not palpable. There were no herniae or masses present. Pelvic examination revealed intact hymen. The genitalia were normal. Rectal examination revealed normal sphincter tone, no tenderness, no evidence of fresh or old blood on the examining finger. Neurological: Abdominal reflexes were absent. All other reflexes were equal and active. Cranial nerves were intact. Objective sensory findings were normal. No pathological reflexes elicited.

Urinalysis: Clear, acid, specific gravity 1.008, negative for albumin, sugar and acetone. There were no pus cells or red cells in the sediment. No casts were seen. Blood count: RBC 4,360,000, hemoglobin 14.5 grams, white count 8,300, 80% polys, 15% lymphs and 5% monos. On smear platelets appeared adequate. Lumbar puncture showed the initial pressure to be 220 mm. and final pressure at 176. Fluid was clear. Spinal fluid protein was reported at 86 mgm.%, mastic 00000. Spinal fluid Wassermann was negative. Spinal fluid sugar was 74 mgm.% and the spinal fluid cell count was 2 lymphs. Blood bromide level showed only a trace present. The NPN was 43 and blood sugar was 121 mgm.%. Electrocardiogram made on admission was not diagnostic. Chest x-ray reported lungs clear except for apical pleural thickening on left. There were sclerotic plaques in the aortic knob. There was mid dorsal scoliosis with convexity to the right. No fractures of rib noted. Skull plate normal, no fracture.

The patient was admitted to the hospital at 1:00 A.M. and slept throughout the night with no complaints, blood pressure remained stable, temperature normal. The following morning the patient's sensorium had cleared and she added the fact that preceding the onset of fainting there was a "crush-

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ing" severe type of substernal pain. However, she does not recall having had similar pain or was there any radiation of the pain. The patient's temperature remained normal during the morning of her first hospital day, she ate a small amount of food and stated that she was feeling better. During the afternoon of the first day the temperature began to rise and reached the level of 100.8° orally. There was no complaint of pain or confusion and the night was spent in comfort. The patient slept fairly well.

At 7:00 A.M. on the morning of the third hospital day the nurse was called, for the patient was having a convulsion. The nursing notes state the patient was cyanotic, face was twitching and respirations were poor. The patient died within five minutes after onset of the convulsion.

Discussed by Dr. William H. Higgins, Jr.*

The pertinent features of this protocol can be summarized as follows: The case is that of a 62 year old white single woman about whose past history little is known. For two years prior to admission to the hospital she had been depressed following the death of her mother. Her family had noted that she was becoming increasingly confused, especially in the morning on awakening and in the afternoon on waking up from the afternoon nap. She apparently had been a nervous woman for it was known that she had been taking bromides.

The patient apparently had been getting along fairly well until the day of admission when she collapsed in her bathroom. An ambulance was called and the ambulance doctor found her to be confused, her blood pressure 100-60, and she was cold and covered with perspiration. She was brought to the hospital and on arrival was still confused and bruises about her head and eyes and conjunctival hemorrhages were found. Positive physical findings included a grade III arteriosclerosis of the vessels of her eye grounds, hard exudates, a few hemorrhages, A-V nicking, and narrowed vessels. Her heart was slightly enlarged by physical examination, the rhythm was regular, the rate 88. A soft apical systolic murmur was heard. Blood pressure was later found to be 120-85. The lungs were clear. The abdomen was negative except for a slightly enlarged liver which was not tender. A thorough neurological examination was done which was entirely negative except for some mental confusion. The neck was not stiff. The laboratory studies were not remarkable. The blood and urine examinations were negative. The blood sugar 121 and the NPN 43. A lumbar puncture was done. No cells were found in the fluid, the spinal fluid protein was slightly elevated, and the pressure was 200 mm of water. An electrocardiogram done on admission was "Non diagnostic". No mention was made of the T Waves, A-V conduction time or axis deviation. The X-rays showed no fractures and only arteriosclerotic plaques in the aorta were seen.

While in the hospital the patient recalled a "crushing" substernal pain which was nonradiating before fainting prior to entry to the hospital. Her course was uneventful and she had no apparent specific treatment. Her temperature rose to 100.8 and otherwise her convalescence was negative. On the third day she had a sudden convulsion, became cyanotic, dyspneic and died.

This protocol can be further summarized as being about a sudden and unexpected death of a 62 year old woman whose main symptoms were mental confusion and syncope and whose positive physical finding was marked arteriosclerosis.

It is fairly definite that this patient had a marked generalized arteriosclerosis. This is brought out by the eye ground changes and the condition of the aorta as seen by X-ray. No comment is made of the condition of the brachial vessels or the pedal pulses. It would be interesting to know about these vessels since they frequently are good indices of the condition of the peripheral blood vessels, especially in arteriosclerosis.

Hypertensive vascular disease is suggested by the finding of the eye grounds and the enlarged heart. However, a persistently low blood pressure, and no mention of left axis deviation or left ventricular strain on the electrocardiogram, and an essentially negative urine all point away from this possibility. The likelihood of a preexisting hypertension will be discussed later.

Only to mention in passing is a disease which is suggested by the eye grounds. In diabetes retinal changes sometimes occur which simulate those found in this patient. Diabetes, however, would in no way explain this patient's clinical picture and this together with the normal blood sugar and negative urine ruled this out.

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More difficult to rule out than hypertension or diabetes are lesions of the brain. The first of these would be a brain injury occurring in the fall with subsequent damage to the brain or a subdural hematoma. These lesions are always difficult to diagnose, however, in this case the X-rays of the skull were negative, the neurological examination was entirely negative for a localized lesion, the patient had no headache, there was no choking of the discs and the spinal fluid was not remarkable.

A brain tumor also seems unlikely in view of the absence of localizing signs, choking of discs, and the sudden terminal convulsion and death. As a rule a brain tumor would be preceded by signs or at any rate coma prior to death.

Subarachnoid hemorrhage must be ruled out in this case. The causes for this disease are many but as a rule they follow the rupture of a congenital aneurysm usually at the Circle of Willis. Hemorrhage from these aneurysms usually occurs in the 3rd or 4th decade and rarely as late as the 6th decade. However, in patients of this age, frequently the cerebral vessels are weakened by arteriosclerotic changes or atheromatous changes which occur in the blood vessels and often hemorrhages may result. Further causes for weakening and later hemorrhage of the cerebral blood vessels would include syphilis, embolic processes, trauma, and certain acute infectious diseases which would include typhoid fever. The clinical picture of subarachnoid hemorrhage is almost invariably headache and dizziness. Eventually these patients become comatosed and almost always their spinal fluid is bloody and they show neurological signs of one type or another. The patient under discussion today, of course, did not have neurological signs or blood in the spinal fluid and her death was sudden without coma. I believe that these would be sufficient to rule out the possibility of subarachnoid hemorrhage.

Cerebral thrombosis should always be considered in any elderly patient who is showing senile changes and finally dies. These people as a rule have localizing signs of one type or another and rarely is their death sudden. The typical onset of a cerebral thrombosis is a gradually occurring weakness of one or more groups of muscles followed usually by reflex changes. The clinical course of this patient seemed to eliminate this possibility.

Cerebral hemorrhage is a good possibility here. Apoplectic strokes notoriously occur suddenly and are frequently associated by a fainting episode or coma. It is common in hypertension and in people with marked arteriosclerosis but is usually associated with convulsions and/or long periods of coma. Bloody spinal fluid and an elevation of the spinal fluid pressure frequently occur although this is not necessary. It would be unlikely for a massive cerebral hemorrhage to occur without localizing signs neurologically or coma.

One final cerebral lesion which would explain in part but not entirely some of the patient's symptoms would be lesions limited to the small blood vessels of the brain. Dr. Walter Alvarez, of the Mayo Clinic, and others have emphasized the frequent occurrence of minute cerebral apoplexies occurring in the cerebral cortex. These small "strokes" are commonly found in elderly people who have prior to death shown sudden personality changes which include irritability, confusion, etc. Frequently these small cerebral hemorrhages are preceded by episodes known as angiospasms which are spastic seizures of the small cerebral vessels. Clinically these people seem to have transient hemiplegias, or in the less severe cases transient episodes of marked confusion or weakness of one or more sets of muscles. Almost invariably after one to twenty-four hours the symptoms entirely subside and the patient is apparently well. These spasms of the small cerebral vessels, however, are frequently associated with localized areas of ischemia which eventually become small degenerative areas which are scattered throughout the brain. A small minute cerebral hemorrhage is frequently found associated with these areas of softening.

Lesions of the heart should next be considered as an explanation for this patient's disease and death. The Stokes-Adams seizure sometimes occurs in elderly arteriosclerotic people. In this condition there is a severe preexisting degenerative disease of the heart such as coronary arteriosclerosis, rheumatic heart disease or syphilitic involvement of the mouth of the coronary. It is usually associated with bradycardia, and manifested by sudden dizzy spells, convulsions, faintness, etc. These people always have the electrocardiographic changes of prolonged A-V conduction time. Occasionally sudden death occurs from cardiac standstill or ventricular fibrillation. This patient, however, had no evidence of brady-

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cardia and we are told that the electrocardiogram showed no changes and we can assume that there was no prolongation of the conduction time.

Aortic stenosis sometimes causes sudden unexplained death. There is no evidence in this case for a preexisting rheumatic heart disease which is the usual cause of aortic stenosis, however, in marked arteriosclerosis the so-called Mönckeberg's sclerosis does occur and a stenosis of the aortic valve follows. There was no evidence, however, by physical examination nor was the blood pressure compatible with aortic stenosis in this case.

Myocardial infarction is an excellent possibility. We recall that the patient has a crushing substernal pain prior to entry to the hospital which was followed by fever. This characterically occurs in many cases of coronary occlusion and death in this case could have followed a new infarct. The patient could also have had an elevated blood pressure which fell following the infarction. This is not at all uncommon and frequently the blood pressure may remain low indefinitely although in the usual case the blood pressure tends to climb gradually several days to a week following the infarction. The majority of cases with coronary occlusion will show electrocardiographic changes, especially if the occlusion is severe enough to cause death. Here we have no evidence of any such change although this does not rule out the possibility nor does it make impossible the occurrence of a second occlusion which caused the terminal event. No mention is made of any arrhythmia which often occurs in severe coronary occlusion. It is also mentioned that the lungs were clear, which one would not expect had the patient had hypertension and a sudden drop of blood pressure because of the infarction. Usually some degree of shock occurs which would, of course, be manifested in part by rales at the lung bases.

The most significant statement in the protocol, I believe, is the final sentence which states that "the patient died within five minutes after the onset of the convulsion". The exact nature of the convulsion was not described and could well have been a terminal spasm rather than a marked severe convulsion such as is seen in epilepsy.

In reviewing the causes of certain deaths which could be applied in this case only one I believe could be a traumatic type. Subdural hematoma would be the only possibility but it would be extraordinarily rare for anyone to have death this suddenly from this cause.

Nontraumatic causes of sudden death possible in this case are also very few. The hemorrhages of the brain such as a hemorrhage into one of the ventricles or a rupture of a vessel at the Circle of Willis almost always result in a deep coma for several hours prior to death. Pulmonary embolism could occur but there is no source known here for the embolus unless it could have come from a mural thrombus. Mural thrombi do not usually occur so soon after infarction and usually presuppose a large or massive infarction for which we have no evidence here. Aortic stenosis may also cause sudden death but it has been ruled out. Ventricular fibrillation or cardiac standstill is usually preceded by some arrhythmia or evidence of heart damage. Rupture of the heart is unlikely here because again there is no evidence of preexisting heart damage. Coronary occlusion, notoriously a cause for sudden death, is an excellent possibility and has already been discussed. Finally, defecting aneurysm as the cause of sudden death is to be considered. Aneurysms of the aorta are usually luetic in origin or are arteriosclerotic. Syphilis has been ruled out but the arteriosclerotic type is an excellent possibility. Those patients usually have a severe pain in the chest which may occur just prior to death or at any interval weeks or months before death which would indicate a partial dissection. As a rule hypertension also accompanies this condition but there are many cases on record which show that following dissection of the aneurysm the blood pressure in the upper extremities drops to normal or even in dissection of the abdominal aorta the blood pressure in the lower extremities may be markedly diminished or disappear entirely. It would be interesting and significant to know in this case that the pulses were present and equal in all four extremities.

In view of the history in this case of a severe crushing type pain substernally, the absence of findings other than those of arteriosclerosis and essentially negative neurological and cardiac findings, and the suddenness of the terminal onset with death following so quickly it seems most likely to me that this patient had a dissecting aneurysm which dissected several days before entry giving her the initial pain and finally at the time of death ruptured with rapid fatal exanguinating hemorrhage.

In summary then I believe that this patient had a

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marked generalized arteriosclerosis, cerebral arteriosclerosis, with possible multiple areas of softening throughout the cerebral cortex and possibly hemorrhages of small cerebral arteries as described by Alvarez. The cerebral cortex will probably show some atrophy. Her death was probably due to a dissecting aneurysm which finally ruptured.

Hospital diagnosis: (1) Dissecting aneurysm.
(2) Generalized arteriosclerosis.

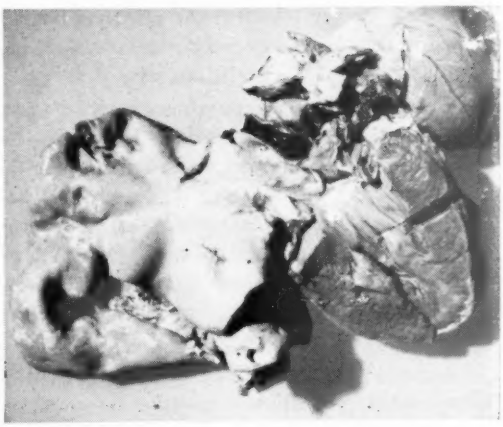
Dr. Higgins' diagnosis: Dissecting aneurysm.

PATHOLOGICAL REPORT: DR. THOMAS M. SCOTTI.*

On opening the thorax about 200 cc. of bloody fluid were noted in each pleural cavity and over 150 cc. of blood in the pericardial sac. The heart weighed 400 gms. The left ventricular wall was hypertrophied, measuring 2 cm. in thickness. The right ventricle measured 0.3 cm. in thickness. There was no valvular disease and the coronary arteries showed moderate atherosclerosis.

The aorta disclosed moderate atherosclerotic change but atheromatous plaques were inconspicious in ascending portion. At a point 4 cm. above the aortic valve there was a somewhat oblique tear in the intima of the anterior wall in the aorta. It was 3 cm. long and was not associated with an atheromatous plaque. The tear extended into the media. There was dissection of the media, along the junction of its outer and middle thirds, which involved the entire circumference of the aorta. This dissection extended downward toward the base of the heart and upward to the mid-portion of the arch of the aorta, involving the innominate artery as far as its bifurcation and from there it extended into the right common carotid artery. There was a considerable amount of freshly clotted blood in the medial dissection. The blood extended into the adventitial layer at the level of the intimal tear producing an extensive hematoma which extended into the subepicardial fibro-adipose tissue overlying both atria of the heart and into the mediastinum, even surrounding the pulmonary arteries and bronchi. In one area overlying the right atrium there was a small defect of the epicardium which was the probable site of escape of blood into the pericardial sac.

Microscopically, sections of aorta and innominate artery showed the dissection of the media by blood. In addition, there were irregular defects of the media characterized by increase in the size of spaces between fibers which were filled with a pale, basophilic, fluid-like substance. There were also areas of fraying of elastic fibers and absence of fibers in other places.



Heart and Aorta. The aorta was opened anteriorly just to the right of the intimal tear which is clearly visualized near the cut edge. The medial dissection is seen best along the right edge of the aorta especially in portions viewed obliquely. Atherosclerotic plaques are more prominent in distal part of arch and descending portion of aorta. Left ventricle is hypertrophied.

Other findings were: Nephrosclerosis, cerebral atherosclerosis, areas of encephalomalacia with reparative cellular reaction involving the left occipital pole and the tip of the left temporal lobe, and mild chronic passive congestion of the liver.

Pathological diagnoses:

Dissecting aneurysm of aorta (ascending and arch).

a) extension into innominate and right common carotid arteries.
b) primary tear in ascending aorta.
c) external rupture producing adventitial hematoma extending
   1) into subepicardial tissues of base of heart leading to hemopericardium (over 150 cc.).
   2) into mediastinum and subsequently bilateral hemothorax (200 cc. each side).

Medial necrosis of aorta.

Myocardial hypertrophy, left ventricular.

Nephorosclerosis.

Atherosclerosis: aorta, coronary and cerebral arteries.

Chronic passive congestion of liver, mild.

Encephalomalacia, focal, left occipital and temporal lobes.

*Assistant Professor of Pathology, Medical College of Virginia, Richmond.

PUBLIC HEALTH

L. J. ROPER, M.D.,
State Health Commissioner of Virginia.

The report of the Bureau of Communicable Disease Control of the State Department of Health for June 1950 as compared with the same month in 1949 and for the period of January through June 1950 as compared with the same period in 1949, is as follows:

	June 1950	June 1949	Jan.-June 1950	Jan.-June 1949
Typhoid and paratyphoid	1	10	29	42
Diarrhea and dysentery	208	231	1,595	1,511
Measles	486	1,646	2,024	20,473
Scarlet fever	51	43	556	400
Diphtheria	10	11	93	72
Poliomyelitis	4	1	19	11
Meningitis	11	6	80	52
Brucellosis	5	4	31	30
Rocky Mountain spotted fever	13	19	17	30
Tularemia	0	5	18	13

FINDINGS OF BLOOD TESTS AS REQUIRED BY VIRGINIA PREMARITAL LAW

The Virginia Premarital Examination Law went into effect on February 28, 1940. Its provisions required, among other things, that a serologic test be taken on all persons applying for a license to marry. It further required that a second serologic test and complete physical examination be performed on all individuals whose initial test indicated that there was a possibility of syphilitic infection.

A recent review of the statistical reports prepared in connection with this law reveals a number of interesting facts. From the date of the passage of the law, through the month of June 1949, 685,044 persons have been tested. Of these, 28,456 persons showed positive blood tests. Therefore 4.6 per cent of the persons tested in connection with application for marriage had positive findings; 526,661 (76.9%) of the applicants were white and 158,383 (23.1%) were non-white. The rate of positive findings among white persons tested was 0.8 per cent; among non-whites it was 15.4 per cent.

The per annum rate of persons with positive findings reached its peak in the war years, totalling 5.6 per cent in the year 1944. There has been a steady decline in the annual rate to the latest figure of 2.9 per cent in 1949. This constitutes a reduction from the peak year to the present year of 48.3 per cent. There has been no significant difference in the trend for whites and non-whites.

Of the total persons tested, 73.6 per cent have been residents of Virginia and 26.4 per cent have been non-residents. The rate for Virginia residents has been consistently higher than the rate for non-residents applying for marriage in the State. This is true equally for whites and non-whites.

In conclusion it may be said that the Virginia Premarital Law has been a good device for finding cases of syphilis, although its effectiveness in this field has been declining. Furthermore, it may be said that this law has provided an excellent source of material which can be used as an indicator for measuring the amount of syphilis existing in one given segment of the population, namely, those persons applying for license to marry.

Increase of 2,266 in Physician Population for 1949.

The net increase in the number of physicians in the United States and its territories and possessions in 1949 was 2,266, according to the 48th Annual Medical Licensure Report of the American Medical Association's Council on Medical Education and Hospitals. (June 3, J.A.M.A.)

These official figures indicate that last year 5,866 physicians were licensed for the first time, and thus represent the gross additions to the profession for that year. In 1949 there were 3,600 deaths of physicians reported to the offices of the American Medical Association.

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MEDICAL SOCIETY OF VIRGINIA

MEDICAL SERVICE COMMITTEE

Medicine in Industry and Its Influence on Medical Care.

The term Industrial Medicine is given many different definitions by physicians and others associated with the practice of medicine. The most common error is to apply the term to medicine as practiced in the coal fields. This is more properly designated "Contract Practice". This type of practice includes only a few of the problems involved in occupational medicine.

The treatment of burns and traumatic injuries are considered by others as the scope of Industrial Medicine. These problems occupy only a small portion of the time of a well-rounded medical program in most large industries. Any industry which requires the full time services of a surgeon is in need of a program of accident prevention.

Occupational medicine is the preferable title for that branch of medicine which has for its purpose the prevention of illness incident to occupations and the improvement of the health status of individuals in industry.

Occupational medicine properly begins with the employment of the individuals. A complete physical examination including urinalysis, indicated blood studies, and a chest x-ray assist in properly placing the new employee. Thus, individuals with hypertension or cardiac lesion will not be assigned to laborious tasks. An annual examination, similar to the pre-placement one, assists the employee in maintaining good health and directly affects the incidence of absenteeism.

Properly designed periodic examinations that will detect the earliest manifestations of toxic substances are a necessity in industries using toxic materials. The frequency of such examinations depends on the nature of the toxic substance to which the employees are exposed. Carelessness in this phase of industrial medicine reflects itself in illness specific for the industry. A good industrial hygiene program is essential for the success of the medical efforts to prevent illness.

Facilities for the treatment of minor illness and injuries may prevent serious illness from situations in which individuals often practice self-treatment. Thus, occupational medicine is largely preventive in its scope and its problems and practice lie principally in the field of internal medicine.

As has been previously indicated, participation by the physician in industry in a good industrial hygiene program is essential. This includes not only the precautions against toxic materials but careful supervision of all cafeteria facilities, ventilation, drinking water, shower and locker rooms, and toilet facilities. This type of program should make employees more health conscious and increase their desire for early medical care. In order to facilitate such care, a program designed for this purpose is important. Industry has many and varied programs for assisting in such matters. Group insurance, continuation of wages and many similar programs are in force. One of the most important of these is hospital care. Inability to meet the financial demand of adequate medical care may superimpose emotional illness. The minimum program in this field should be to encourage enlistment in some type of hospital plan—either Blue Cross and Blue Shield or some plan which provides similar benefits. Such efforts on the part of industry cannot help but elevate the health standards of the community and assist in solving the great problem of medical care.

C. L. SAVAGE, M.D.,
Waynesboro, Virginia

MENTAL HEALTH

Joseph E. Barrett, M.D.,
Commissioner, Department of Mental Hygiene and Hospitals.

Child Guidance Clinics.

Special clinics caring for children with emotional problems have been in existence in this country since 1909. At that time, Healy founded the Chicago Juvenile Psychopathic Institute (now known as the Institute for Juvenile Research). He made use of the professional services of the psychiatrist, the clinical psychologist and the psychiatric social worker in attacking the problems of children. Southard, at the Boston Psychopathic Hospital which was started in 1912, introduced the term "clinical team" to describe the collaborative activities of these professional groups. The term, "child guidance clinic", was coined in 1922 and was used by the Division on the Prevention of Delinquency of the National Committee for Mental Hygiene in demonstration clinics supported financially by the Commonwealth Fund.

The initial emphasis was on the prevention of delinquency but later the goals were (a) adequate and correct diagnosis, (b) manipulation of the environment in terms of the needs of the child and lastly, the treating of the child in his usual environments.

At present there are three child guidance clinics in our Virginia system. The Memorial Guidance Clinic in Richmond has recently celebrated its twenty-fifth anniversary. The Children's Service Center of Charlottesville and Albemarle County was begun in 1947, while the Fairfax County Child Guidance Center at Falls Church has been opened more recently.

In these, as in other child guidance clinics, the focus is on the child and on his problems. Children are referred to these clinics who show such symptoms as feeding disturbances, tantrums, enuresis, persistent thumb sucking, night terrors, poor school achievement, lying, truancy, stealing, excessive daydreaming, over-aggressiveness, etc. Children and adolescents up to the age of eighteen are usually accepted but the majority of referrals are in the preadolescent group.

The emphasis in these clinics is on treatment. Obvious cases of gross mental deficiency, and children suffering only from neurological disorders, are not usually referred to these particular clinics.

Before a child is accepted for treatment, the parent is given an appointment for an intake interview with the psychiatric social worker. This case worker, who has had postgraduate work in psychiatry and sociology and has a Master's degree from a special school of psychiatric social work, has been trained in interviewing techniques. She has acquired special skill in securing from the parent not only the necessary medical and psychiatric history of the patient, but also the emotional feelings and attitudes of the parent toward the child, and toward other members of the family.

At one time the psychiatric social worker worked chiefly with the parent or parents and did "environmental manipulation". This function is now greatly diminished and her function is more that of a psychotherapist who deals with feelings and attitudes and who attempts "attitude therapy", i.e., to modify and/or correct the parents' attitude to the child and his problems.

The clinical psychologist is one who has had postgraduate work in general and also in abnormal psychology, and has either a M.A. or Ph.D. degree. He is not only skilled in administering various psychological tests to measure intelligence, but also administers personality tests, such as the Rorschach, T.A.T. (Thematic Apperception Test), etc. The clinical psychologist is also trained in research techniques and may do a certain amount of psychotherapy with the child; such treatment is done under the close supervision of the psychiatrist.

The psychiatrist heading a child guidance clinic is required to have a medical internship and a psychiatric residency, as well as a minimum of two years special training in child psychiatry.

If a physician wishes to refer a case to a child guidance clinic, he should prepare the parents in advance for this referral. Parents often become indignant when the physician makes an appointment for them at such a clinic and the family then learns that it is a psychiatric clinic. Sometimes such parents, resenting the implication of mental illness,

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neither accept treatment in the clinic nor ever return to the referring physician.

When an appointment is made, the parent is told to come without the child and that he is to be interviewed by the social worker. At the intake interview the trained worker obtains a history from the parent, describes the manner in which the clinic operates, and attempts to evaluate whether or not the child is a suitable case for treatment. If the case appears suitable, both parents are told that they will be expected to come for treatment once a week, that while the child is having treatment by one staff member (usually the psychiatrist), the parent is to be having psychotherapeutic sessions with another staff member (usually a psychiatric social worker).

Before the child sees his therapist he has one or more appointments with the clinical psychologist who gives him intelligence tests, projective technique tests, etc.

In one of our clinics (Charlottesville) we use the principle that the most disturbed member of the family should be treated by the available staff member who has the greatest skill and professional experience. We also take into consideration the need of the child to work with a woman versus a man therapist. Thus, at times the psychiatrist may treat the child, the father or the mother. The clinical psychologist or the psychiatric social worker may treat the child or the parent.

Treatment of emotional disorders of children may require at least six months. Occasionally a child's symptoms may disappear within a few weeks after onset of treatment; on the other hand, children with physical complaints of psychogenic origin may cling to their symptoms indefinitely and may require one to two years of treatment.

Because of the limited number of personnel trained to work in child guidance clinics, the clinics in this, as in other states, have been forced to create waiting lists. This means that after a physician refers a child to such a clinic, the child may not be accepted for treatment for several months. Referring physicians are often disturbed about this waiting list and may try to bring pressure on clinic staff personnel to have their patient taken out of turn, or request that their patient be given diagnostic surveys.

The emphasis in child guidance clinics is on treatment, and not on diagnosis. For this reason, until more psychiatrists, psychiatric social workers and clinical psychologists are trained to work with children, it will be necessary to either maintain a waiting list or to provide inadequate and incomplete therapy for the child.

BOOK ANNOUNCEMENTS

You and Your Heart. A Clinic for Laymen on the Heart and Circulation. By H. M. MARVIN, M.D., and T. DUCKETT JONES, M.D., IRVINE H. PAGE, M.D., IRVING S. WRIGHT, M.D., DAVID D. RUTSTEIN, M.D. Foreword by Paul D. White, M.D. Random House, New York. 1950. xi-306 pages. Illustrated. Cloth. Price $3.00.

This volume was written for persons lacking medical background, but "in order to ensure clarity" the original manuscript of the physician-authors was "translated by a nonmedical writer into language that could not be misunderstood by lay readers." As stated in the introduction, "this is not a self-help book, designed to enable the reader to make diagnoses and prescribe treatment. Its chief purpose is to bring some measure of enlightenment and understanding" of cardio-vascular diseases "to all who read it, and a great comfort to many who have suffered needless anxiety through misunderstanding or lack of knowledge." Another purpose, no less laudable though somewhat more subtle, is to stimulate interest in the current efforts of the American Heart Association to foster more research, promulgate knowledge, and coordinate various health activities pertaining to the care of cardio-vascular patients.

The subject matter is reasonably comprehensive and, though most problems are viewed through distinctly rose-colored glasses, that is designedly so and as it should be. The doctor can safely recommend this book to his adult cardiacs and to the parents of younger ones in the secure knowledge that those who read it should profit thereby.

EDWARD A. DELARUE, JR., M.D.

The Practice of Medicine. By JONATHAN CAMPBELL MEAKINS, C.B.E., M.D., LL.D., D.Sc., formerly Professor of Medicine and Director of the Department of Medicine, McGill University; Formerly Physician-in-Chief, Royal Victoria Hospital, Montreal; Formerly Professor of Therapeutics and Clinical Medicine, University of Edinburg; etc. Fifth Edition. St. Louis, The C. V. Mosby Company. 1950. xx-1558 pages. With 518 illustrations including 50 in color. Cloth. Price $13.50.

EDITORIAL

William Crawford Gorgas (1854-1920)

PROVIDENCE or fate played a large role in developing the specialty of sanitary engineering. The sanitarian needed a spectacular disease for demonstration of his skill. An ordinary disease like malaria, even though it were more widespread, and actually killed more people, would not do. Nature supplied such a disease in yellow fever, a disease that had been endemic for more than two centuries in nearby Havana. Like syphilis it has been called an American disease, but medical historians have expressed grave doubts that either disease had its origin in the Western Hemisphere. However, both became firmly established in North America and Havana became the permanent focus from which the yellow jack invaded the sea ports of the United States at frequent intervals. Like other great epidemics it was carried by trade and destroyed commerce. Like the plague of the Renaissance it was the subject of much "literature" so that at its approach people fled in such numbers that few were left to bury the dead. Unlike other epidemic diseases it spread in mysterious ways and evaded the strictest quarantine. It defied all known means of control. It defeated victorious armies—the English in 1762 and Napoleon's picked troops in 1800, and was in a fair way of doing the same to the American Army of occupation of Cuba in 1900.

At the end of the Spanish-American War, Major Gorgas was put in charge of sanitation in Havana. The city was filthy according to the sanitary standards of the times and he set about cleaning it up. He soon had it as clean as any in the temperate zone. Intestinal diseases were greatly reduced but, much to the chagrin of the United States Army, yellow fever began to increase. The reason now is perfectly plain—the improved sanitary conditions of Havana had attracted many non-immune persons. The situation was becoming serious so the War Department sent down a special commission headed by Walter Reed (see previous chapter, *Virginia Med. Month.* 76:423, 1949) and in the course of months the mystery was solved. Carlos Findley, a Havana physician, by careful observation of the habits and distribution of the Stegomyia mosquito, had known since 1881 that this mosquito was the carrier of the disease, but was unable to prove it to the satisfaction of anyone else. He actually performed some inoculation experiments with his infected mosquitoes which failed. Henry R. Carter, an U.S. Public Health quarantine officer, demonstrated what the otherwise accurate observations of Findley had overlooked. Carter, with accurate records that he had kept of outbreaks of the disease in the Gulf States, showed that there was a time lag of some ten days before a new case became infectious. He called this "extrinsic incubation." Reed and his co-workers proceeded to demonstrate the truth of Findley's and Carter's theories. They proved that the Stegomyia mosquito was the culprit, but that she was innocuous until the virus of the disease had time to develop in her body, a period of several days. After this period of "extrinsic incubation" she became the most deadly of all animals. The problem then was how to get rid of the Aëdes aegypti, as this species is now called.

The yellow fever mosquito has one weak side. It is a domesticated insect, living only in and about human habitations. The female does not lay her eggs until she has fed upon human blood and then only in water contained in man-made vessels. It was then only necessary to keep a film of petroleum on the surface of water in rain barrels or otherwise mosquito proof them and to drain all the tin cans and other vessels containing useless water. This was considered to be an impossible task in Havana.

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It certainly required great tact, patience, and perseverance. Gorgas was the man and he was on the spot. Even his name was a help for it had a Spanish sound.

Fate seemed determined to raise and train a proper adversary for the yellow jack, even supplying a proper prenatal background. Josiah Gorgas, who later became Chief Ordinance Officer of the Confederacy, was born at Myerstown, Pennsylvania, educated at West Point, and in the Mexican War, went as 1st Lieutenant to Vera Cruz. Here he contracted yellow fever. In 1853 he was in command of the arsenal at Mount Vernon near Mobile. Mount Vernon was high and dry and was a safe place to go when epidemics broke out in Mobile. In 1853 a severe epidemic visited Mobile and for that reason Amelia Gayle, daughter of Governor John Gayle, visited her uncle, Dr. Matthew Gayle, who lived next door to Gorgas' headquarters. Before the end of the year they were married and on October 3, 1854 William Crawford Gorgas was born. His birth was attended by Dr. Josiah Nott the celebrated doctor of Mobile who was one of the first to suggest that mosquitoes carried yellow fever.

Young William Gorgas, raised as he was in military atmosphere and spending the impressionable years between seven and eleven in the Capitol of the Confederacy, was determined to follow his father's career. Failing to get an appointment to West Point, he chose the only other way of becoming an officer in the United States Army i.e., medicine. His father, who had a poor opinion of Army doctors, advised against it but finally consented and, thus fatefully, William Crawford Gorgas became a medical student at Bellevue and in due time an officer in the United States Army. Yellow fever was destined to play a role in his own marriage, as it had done previously in that of his father's.

In 1882 Dr. Gorgas was assigned to Fort Brown with strict orders to avoid contact with yellow fever patients. He disobeyed these orders and was caught performing an autopsy on a yellow fever victim. He was arrested and court martialled and sentenced to the quarantine part of the Fort. The sentence was commuted after a few days. However, he contracted the disease as did his future wife, Miss Marie Doughty, who was visiting the family of the Commandant when Gorgas was sent to Fort Brown. After this, being immune, he was sent by the government wherever yellow fever appeared. It was not long before he had a reputation of being an expert on the disease. In 1898 he became chief sanitary officer in Havana, and when the Reed Commission made its report in 1901 his great hour had arrived. He freed Havana of yellow fever more quickly than he expected and turned his attention to the more difficult task of the control of malaria. His successes in Havana led to his appointment as head of the sanitary forces in the Panama Canal Zone. Here he lacked support of the engineers in charge of the work and his task was extremely difficult. With the small force of sanitarians at his command he concentrated on the mosquito and neglected garbage and smells. This was more than the old line engineers could stand. Complaints were lodged against him in Washington. On one occasion he came very near being supplanted by an osteopath, and on another by an English sanitarian. In 1906 the American Medical Association unofficially sent Dr. Charles A. L. Reed of Cincinnati, to investigate conditions on the isthmus. His report supported Gorgas' administration in every way. Matters came to a head when the Secretary of War demanded of the President, Theodore Roosevelt, that Gorgas be replaced. Mr. Roosevelt turned to Dr. Alexander Lambert of New York for advice. Lambert convinced the President that the success of building the canal depended on getting rid of yellow fever and that in turn depended on eradicating the Aëdes aegypti. Gorgas was not removed, but instead the President told the Commissioner he must get behind Gorgas. After that his task was greatly simplified.

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Not only did Gorgas prove to the world that the white man could live safely and happily in the tropics but he convinced the world of the value of sanitary engineering. He was promoted to Surgeon-General which position he filled during the 1st World War. Upon reaching the retiring age he joined the Rockefeller Foundation in the project of eradicating yellow fever from the entire world. In 1902 he was on his way to investigate the rumor that there was still a focus of yellow fever in West Africa when he had a cerebral accident. He died in London, loaded down with honors and honorary degrees.

It should interest the readers of the *Monthly* to know that two of the principals, in this story, Reed and Carter, were Virginians, and a third, Gorgas, spent the impressionable years of his life in Richmond.

This is the 15th of a series "Doctors for whom the public should be thankful."

Rocky Mountain Medical Association

IN 1871 the American Medical Association met in San Francisco. This is the first time the A.M.A. had met on the Pacific Coast. In fact, only once had it been west of the Mississippi and that was in 1854 when it met in St. Louis. The journey was described as exhausting. In many other ways there were great differences. There was in 1871 no Journal of the Medical Association. Massachusetts and California reported that they had established departments of State medicine. The previous year the Association passed a resolution urging the Government to establish a national medical school. The association also wanted the Government to grow cinchona trees. In San Francisco, the President, Dr. Stille, lamented the fact that women had entered the ranks of the medical profession and doubted the wisdom of the move. This discussion was continued at the next annual session when Dr. D. W. Yandell in his presidential address came to the defense of the women. The delegates went to California in "palace cars", and there were no telephones in existence although the telegraph had been in use for about 25 years.

Rail transportation to the Pacific Coast began in 1869. For 123 physicians to make a trip across the Rockies in May, 1871 to attend a medical meeting in San Francisco was therefore considered quite a feat. To properly commemorate the event, these physicians organized a special society, the Rocky Mountain Medical Association.

The ladies who made the trip and the "few gentlemen who accompanied them" were made honorary members. The purpose of the Association was to meet once a year when the American Medical Association met, have a dinner together and listen to an address by their President. The first President was Dr. Washington Atlee. Dr. John Morris of Baltimore was Secretary and Treasurer. The addresses of the first four Presidents consisted mainly of anecdotes on medicine in general and on western travel in particular. Reminiscences of the long and arduous trip occupied a prominent part of the presidential addresses. The fifth President of the Association was Dr. J. M. Toner. His address was an account of the archæology of the country and a very complete description of Indian medicine with an excellent bibliography. It occupies 106 pages of the transactions of the Rocky Mountain Medical Association. Dr. N. S. Davis was elected sixth President. This is the last of the printed record of the Rocky Mountain Medical Association. Whether it survived Dr. Toner's address, or whether Dr. Davis ever held office, we have not been able to learn. There is no trace of a second volume of Transactions.

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The Ninety-Ninth Annual Meeting of the American Medical Association June 26-30, 1950

MARK TWAIN was always enthusiastic about the badness of San Francisco weather, so we went prepared for anything. Evidently San Franciscans save up their perfect weather for A. M. A. conventions, for we had nothing but invigorating sunshine at just the right temperature. The San Franciscans are fine looking, sprightly people who look like they are having a good time. They dress well and eat well, and it is a pleasure to be with them.

An American Medical Association convention is a five-ring educational circus; with a scientific assembly, general meetings, motion pictures and television, technical and scientific exhibits, in addition to the business meetings of the House of Delegates. It seemed to us that the exhibits this year were not quite up to the usual standard. It may be that there were so many that we could not take them all in. Having the exhibits on three different levels is a distinct disadvantage to the aging portion of the membership.

The sectional meetings were well attended. They still form a valuable part of the convention. We were fortunate to hear two section chairman addresses. Dr. James R. Bloss of the Section on Obstetrics and Gynecology spoke on the causes of fear among obstetrical patients. Dr. Frederic W. Clement of the Section on Anesthesiology spoke on surgery before there was any anesthesia.

Among Virginians honored at the meeting was Dr. Russell L. Haden, who was elected to the Council on Medical Education and Hospitals. Dr. Walter B. Martin is an A. M. A. trustee.

The next clinical session will be held in Cleveland, December 5-8. It was to have been held in Denver but, on account of delays in construction of its auditorium, Denver had to withdraw its invitation.

SOCIETY PROCEEDINGS

Williamsburg-James City County Medical Society.

A called meeting was held in Williamsburg, June 16. After a dinner and social period the meeting was called to order by Dr. Eleanor H. Beamer-Maxwell, president. Fourteen members were present.

Dr. Joseph E. Barrett was selected as delegate to the meeting of the Medical Society of Virginia to be held at Roanoke in October. Dr. Beamer-Maxwell was designated as alternate.

After discussion of a matter which was referred to the Membership committee, the new president, Dr. Beamer-Maxwell, presented a list of committee appointments: Dr. Gordon Keppel, chairman of program committee; Dr. Frank A. Dick, chairman of membership committee; Dr. Joseph E. Barrett, chairman of special committee to carry out the ceremony of erecting a memorial plaque at Jamestown. Dr. Beamer-Maxwell pointed out that the constitution does not provide for a grievance committee as a standing committee, and asked instructions from the society. The society voted that the president would be authorized to appoint a special committee, to consider grievances when and if they are presented, to consist of three members to serve at the pleasure of the president.

The meeting adjourned until the next meeting on September 15, 1950.

Dr. Granville L. Jones of Williamsburg is secretary of the Society.

Wise County Medical Society.

There was an unusually good meeting of this Society on June 14th, with Dr. W. B. Barton of Stonega presiding. Thirty-three physicians and several visitors were in attendance. The meeting was held at Hotel Norton in Norton and, following a social hour, a country style steak dinner was enjoyed, Dutch treat. Dr. J. A. Pettigrew of Dunbar was elected to membership.

The guest speakers were Dr. B. M. Overholt,

whose subject was The Peptic Ulcer Syndrome, and Dr. Herbert Acuff, who spoke on Lesions of the Colon, with Diagnosis and Management. Both speakers are of the Acuff Clinic, Knoxville, Tenn.

NEWS

University of Virginia, Department of Medicine, Commencement.

Exercises incident to the commencement of the medical as well as other departments of the University of Virginia were held on June 9 to 12 inclusive. A feature of the celebration was a housewarming in the remodeled and enlarged Alumni Hall for all alumni. Dr. Vernon W. Lippard, dean of the Department of Medicine, told the medical alumni of the changes in the medical curriculum to be effective next Fall. Golf, the annual barbecue and dances added to the social features. The baccalaureate address by Dr. Joseph Sittler, Jr., of the Chicago Lutheran Theological Seminary, class day exercises, and a reception by President and Mrs. Colgate W. Darden, Jr., completed Sunday's program. The graduating exercises and conferring of degrees took place in McIntire Amphitheater on Monday, with the final ball that evening.

The list of medical graduates with their hospital appointments follows:

University of Virginia Hospital, Charlottesville: Drs. Ivan Hays Bush, Reedy, W. Va.; John Baldwin Catlett, Richmond; Marion Dees Faris, Charlotte, N. C.; Warren Collins Gregory, Atlanta, Ga.; Rozelle Hahn, Columbus, Miss.; Seth Guilford Hobart, Charlottesville; Paul Randall Marsh, Charlottesville; Samuel Edmund Miller, Lexington; James Cipriano Respess, Norfolk; E. A. Sawada, Agana, Guam; Frank Eugene Taylor, Richmond; and James Burnley Wood, Charlottesville.

Memorial and Crippled Children's Hospital, Roanoke: Drs. Everett Lee Coffey and Walter Buhrman Garland, Jr., both of Roanoke.

De Paul Hospital, Norfolk: Drs. Fred Selden Cruser, William Henry Romm, and James Mounts Wolcott, Jr., Norfolk, and Thomas Marion Hall, Richmond.

Blue Ridge Sanatorium, Charlottesville: Dr. James Andrew DeLozier, Boyds Creek, Tenn.

U. S. Naval Hospital, Portsmouth: Dr. Charles Old Barclay, Jr., Portsmouth.

Duke University Hospital, Durham, N. C.: Drs. Robert Sims Caldwell, Baldwyn, Miss., and Reginald Buchanan Henry, Jr., Norfolk.

Santa Barbara Cottage Hospital, Santa Barbara, Calif.: Dr. William Russell Brooks, Radford.

U. S. Naval Hospital, San Diego, Calif.: Drs. James Campbell Cantrill, Georgetown, Ky., and Joseph Leon Schwartz, Jr., Charlottesville.

Fitzsimons General Hospital, Denver, Col.: Dr. George Allen Buckmaster, Akron, Ohio.

Johns Hopkins Hospital, Baltimore, Md.: Drs. James Colvin Causey, Lester Manor, and John Archibald Campbell Colston, Jr., Baltimore, Md.

Union Memorial Hospital, Baltimore, Md.: Drs. Clarence Brock Trower, Jr., Norfolk, and Josiah Frederick Reed, Jr., Harrisburg, Pa.

Bayamon Puerto Rico Hospital, Bayamon, P. R.: Dr. Cristino Manuel Colon-Betances, Rio Piedras, P. R.

Presbyterian Hospital, San Juan, P. R.: Dr. Gladys Pietri-Oma Sutherland, San Germain, P. R.

Strong Memorial Hospital, Rochester, N. Y.: Drs. Paul Tulane Craddock, Lynchburg, and Glenn Brady Updike, Jr., Danville.

New York Postgraduate Hospital, New York, N. Y.: Dr. Harrison Fertig, Plainfield, N. J.

Beth Israel Hospital, New York, N. Y.: Dr. Robert Louis Rowan, Brooklyn, N. Y.

U. S. Naval Hospital, St. Albans, N. Y.: Dr. Benjamin Price Riley, Jr., New York, N. Y.

Beth Israel Hospital, Boston, Mass.: Dr. Robert Jerold Frank, Newport News.

U. S. Marine Hospital, U.S. P. H. S., Seattle, Wash.: Drs. Claude Robertson Garfield, Arlington, and Theodore Lathers Marks, Queens Village, N. Y.

Queens Hospital, Honolulu, T. H.: Dr. Lawrence Noah Gilliam, Wise.

Tripler General Hospital, Honolulu, T. H.: Richard Eugene Rankin, Mount Holly, N. C.

Charity Hospital, New Orleans, La.: Drs. George William Herring, Meridian, Miss., and Robert Edgar Mitchell, Jr., Richmond.

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Minneapolis General Hospital, Minneapolis, Minn.: Dr. Guy Foster Hollifield, Martinsville.

Medical Branch, University of Texas, Dallas, Texas: Dr. James Morrison Hutcheson, Jr., Richmond.

Parkland Hospital, Dallas, Texas: Dr. Elmer Oswald Smith, Jr., Alexandria.

Indiana University Medical Center, Indianapolis, Ind.: Dr. Patricia Ann Lawrence, Charlotte, N. C.

Georgetown University Hospital, Washington, D. C.: Dr. Edward Joseph Mears, Norfolk.

Indianapolis General Hospital, Indianapolis, Ind.: Dr. Rupert Wilson Quaintance, Jr., Slate Mills.

Robert Packer Hospital, Sayre, Pa.: Dr. Beryl Macy Oser, Newport News.

Barnes Hospital, St. Louis, Mo.: Drs. Dorothy Louella Reycroft, Monessen, Pa., and Paul Howard Wornom, Dare.

Jefferson-Hillman Hospital, Birmingham, Ala.: Dr. John Kenneth Robertson, Winston-Salem, N. C.

Cincinnati General Hospital, Cincinnati, O.: Dr. David Valentine Strider, Charles Town, W. Va.

Hartford Hospital, Hartford, Conn.: Dr. Elliott Boyd Sweet, West Hartford, Conn.

Grace-New Haven Community Hospital, (New Haven Unit) New Haven, Conn.: Dr. William Geoffrey Wysor, Jr., Richmond.

University of Michigan Hospital, Ann Arbor, Mich.: Dr. Bruce Edward Toppin, New Castle, Ind.

Delaware Hospital, Wilmington, Del.: Dr. Charles William Wagner, Wilmington, Del.

Borderline Licensure.

Section 54-274 of the Code of Virginia makes it unlawful for any person to practice in Virginia without a license. However, a Virginia license is not required of a person residing on the border of a neighboring State or the District of Columbia who is licensed to practice in the state or district of residence if the following conditions are met: (1) The practitioner has satisfied the Virginia Board of Medical Examiners that he is eligible for such practice, has registered with the Board, paid the fee of one dollar, and obtained a certificate to practice: (2) he does not open an office or appoint a place in Virginia to meet his patients or receive calls: (3) the state or district in which he resides has extended a similar privilege to persons licensed in Virginia.

The certificate of registration shall be renewed each year, and the annual fee of one dollar paid.

Scientific Exhibits

Very excellent and ample space for the Scientific Exhibits at the Hotel Roanoke has been assigned to the Exhibit Committee. The same decorating firm which furnished the booths last year will again service us. Those who saw the exhibits last year will remember the same equipment is furnished as is used at the A.M.A. Viewing boxes for transparencies are also furnished which are fitted with fluorescent lights.

In order to secure desirable space, all exhibitors are requested to write the Chairman of the Scientific Exhibit Committee, Charles H. Peterson, M.D., 603 Medical Arts Building, Roanoke, Va., for application blanks as soon as possible. This will enable the committee to "block out" the space more efficiently.

Special Service by a Component Society.

The Alexandria Medical Society is aware of the fact that medical emergencies do arise wherein one's personal physician may not be available immediately. Also, in cases of transient and recent residents, there may not be a personal physician on whom they may call. Therefore, it is the desire of the Alexandria Medical Society that emergency medical care be available to the citizens of Alexandria at all times. On July 1, 1950, the local medical society is initiating a service to provide emergency care. This type of service has been successfully established by other medical societies throughout the country.

To simplify and accelerate the obtaining of an emergency physician, the Alexandria Medical Society has set up a switchboard which will be staffed 24 hours a day the year round. The switchboard is listed under the name of the Alexandria Medical Society. Individuals in need of this service merely have to call this number and they will be directed to the doctor or doctors on call.

Recent residents of the Alexandria area may obtain names of physicians for other than emergency services, as well as the names of specialists in the various medical fields by calling that Society.

The Alexandria Medical Society has organized and is financing these services to make sure that no one in the city of Alexandria and environments will lack medical attention.

Dr. Henry Chesley Decker,

Class of '47, Medical College of Virginia, has just completed a residency in internal medicine at Woman's Hospital, Baltimore, and he and his wife have come back to Richmond to make their home. He will first serve a residency in internal medicine at Johnston Willis Hospital after which he will be associated with his father, Dr. H. W. Decker, of this city.

Mathews County Has First Hospital.

Dr. William A. Sadler of Mathews has opened his maternity hospital in that town, though the work will not be limited to obstetrics. He will have the assistance of his wife, the former Lynn Mapp Powell as general supervisor. She is a graduate nurse from Elizabeth Buxton Hospital, Newport News, and was formerly obstetrical supervisor there.

Dr. and Mrs. W. Ambrose McGee

And children left Richmond the middle of July to make their future home in Palm Beach, Florida, where Dr. McGee will limit his practice to allergy. Upon leaving Richmond, he will stop at Saluda, N. C., where he will lecture in the Pediatric Seminar as he has for several years.

The American College of Physicians

Will conduct its 32nd annual session at St. Louis, Mo., April 9-13, inclusive, 1951. Dr. Ralph Kinsella of St. Louis is the General Chairman and will be responsible for local arrangements and for the program of Clinics and Panel Discussions. Dr. William S. Middleton, President of the College, Madison, Wis., will be in charge of the program of morning lectures and afternoon general sessions.

Grants for Cancer Research in Hospitals.

Virginia's two medical schools have been included in grants made by the National Cancer Institute for supporting cancer research in hospitals, universities and other non-Federal institutions. They were made upon the recommendation by the National Advisory Cancer Council and the approval of Surgeon General Leonard A. Schele of the Public Health Service. The project directors in Virginia allowed this grant are Dr. George Zur Williams and Dr. Nelson F. Young at the Medical College of Virginia, and Dr. H. Rowland Pearsall at the University of Virginia.

Dr. Frank Blanton,

Class of '46, University of Virginia, Department of Medicine, son of Dr. and Mrs. Wyndham Blanton of this city, is locating in Richmond where he will be an assistant resident at the Medical College of Virginia Hospital. He recently completed a residency at Strong Memorial Hospital, Rochester, N. Y.

Dr. Charles E. Llewellyn, Jr.,

Of Richmond, has gone to Denver, Colorado, where he will be one of the resident physicians at the Colorado General Hospital. His wife accompanied him.

Dr. J. M. Dixon

Of Roanoke has been selected as a Fellow by the Heed Ophthalmic Foundation, and will do research and study at Harvard, Columbia and Northwestern Universities with Drs. Dunphy, Dunnington and Vail.

In June, Dr. Dixon presented a paper at the meeting of the Association for Research in Ophthalmology held in San Francisco.

Award for Outstanding Research in the Field of Infertility.

The American Society for the Study of Sterility offers an annual award of $1000 known as the Ortho Award, for an outstanding contribution to the subject of infertility and sterility. Competition is open to those in clinical practice as well as individuals whose work is restricted to research in the basic sciences. Essays submitted for the 1951 contest must be received not later than March 1, 1951. The Prize Essay will appear on the program of the 1951 meeting of the Society. For full particulars, address The American Society for the Study of Sterility, 20 Magnolia Terrace, Springfield, Mass.

Advertisements in Your Journal Are A-1.

Advertisers in our journal are carefully selected. Only those meeting our advertising standards may use the facilities of our pages. No advertisement will be accepted which, either by intent or inference, would result in misleading the reader. May we suggest that you review the ads in each issue of our journal and, when occasion arises to prescribe products featured or use the facilities offered, tell them you saw their ad in the *Virginia Medical Monthly*.

Dr. A. L. Herring, Jr.,

Returned to Richmond, July 1st, after having served a six-months fellowship in pathology in the laboratory of Dr. Shields Warren at New England Deaconess Hospital, Boston. He will be engaged in

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the practice of general surgery at Grace Hospital in Richmond.

Health Information Foundation.

This organization, launched early in the year, is devoted to the betterment of health of the nation by means of a continuing study of the nation's health facilities. It is being financed by members of the pharmaceutical, drug and allied industries. Admiral William H. P. Blandy, who was in charge of atomic bomb tests at Bikini and recently retired from the position of Commander-in-Chief of the Atlantic Fleet, is president of the organization, and John G. Searle, president of G. D. Searle & Company of Chicago, is chairman of the Board. The officers and directors of the Foundation are officers in many of the leading pharmaceutical and other industries, all interested in the nation's health facilities and the collection and distribution of information as to methods of protecting individuals and their families against financial hardships of sickness and accident. It encourages the use of health services and hospitalization on a voluntary prepayment basis.

Dr. H. L. Baptist,

For many years of Ivy Depot, but more recently of Granite Quarry, North Carolina, has retired from practice and has returned to Virginia. He is now living at Gloucester Point.

News from University of Virginia Department of Medicine.

Dr. John Hamilton Allan, formerly associated with the School of Medicine of the University of Pennsylvania, has joined the faculty of the Department of Medicine of the University of Virginia as Professor and Chairman of the School of Orthopedics.

Dr. Joseph F. A. McManus, formerly associate professor of Pathology at the Medical College of Alabama, has joined the faculty of the University as associate professor of Pathology.

Dr. Morris Sullivan McKeehan, formerly associated with the Department of Zoology, University of Chicago, will join the School of Anatomy, University of Virginia, on September 1st as assistant professor of Anatomy.

Dr. Paxton Stodder, formerly intern in Medicine at the Massachusetts Memorial Hospital, has been appointed Instructor in Pharmacology at the University of Virginia.

Dr. Thomas Warren has been appointed Instructor in Clinical Pathology at the University.

The following former members of the resident staff of the University of Virginia Hospital have been appointed full-time instructors in the Department of Medicine:

Dr. Dwight Brown—Obstetrics & Gynecology
Dr. Samuel Hay—Internal Medicine
Dr. Robert Kelley—Urology
Dr. Carey Moon—Otolaryngology

The following promotions in the Faculty of Medicine, University of Virginia Department of Medicine, are announced:

Dr. William Norman Thornton, Jr., from associate professor to Professor and Chairman of the School of Obstetrics and Gynecology.

Dr. Oliver B. Bobbitt, from Instructor to Assistant Professor of Clinical Pathology.

The annual meeting of the University of Virginia Alumni Association was held on June 9th with an attendance of approximately 150. Dr. Edward F. Bland, Class of 1927, associate in medicine at Harvard Medical School and Physician to the Massachusetts General Hospital, gave the annual address by an alumnus. Other papers on the scientific program were presented by members of the Medical Faculty. President Colgate W. Darden, Jr., and Dr. Seale Harris of Birmingham, Alabama, spoke at the dinner.

Dr. Dudley C. Smith, Professor of Dermatology and Syphilology, has been elected Chairman of the Section on Dermatology and Syphilology of the American Medical Association for 1950-1951.

Contracts have been let for erection of the unit for research and treatment in the field of cancer. Total cost of the project is approximately $250,000.

The International College of Surgeons,

United States Chapter, will hold its fifteenth Annual Assembly and Convocation in Cleveland, Ohio, October 31, November 1, 2, 3.

The program will include scientific sessions on subjects in the fields of general surgery; eye, ear, nose and throat surgery; gynecology and obstetrics; urology; and orthopedic, thoracic, plastic and neurological surgery. In addition, an extensive technical and scientific exhibit will be presented by lead-

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ing manufacturers of surgical instruments, x-ray apparatus, operating room and hospital equipment, pharmaceuticals and others. Special entertainment for the doctors' ladies has been planned. Several hundred surgeons will be received as Associates and Fellows of the International College at the Convocation to be held in the Cleveland Public Auditorium, November 3.

All doctors of medicine interested in surgery and its advancement are invited to attend, and can obtain a program upon request to Arnold S. Jackson, M.D., Secretary, Jackson Clinic, Madison 4, Wisconsin. For hotel reservations, contact Committee on Hotels, International College of Surgeons, U.S. Chapter, 511 Terminal Building, Cleveland 13, Ohio.

Conference on Cortisone.

Dr. Tom D. Spies, Dr. Robert E. Stone, Dr. Samuel Dreizen, and other members of the staff of the Nutrition Clinic, Hillman Hospital, Birmingham, conducted on June 13, an all-day Conference on Cortisone, the first of its kind even to be held. Some four hundred physicians attended the Conference from Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina and Tennessee.

Married.

Dr. Mortimer Lee Williams, son of Dr. and Mrs. Mortimer H. Williams of Roanoke, and Miss Shirley Sawyer, daughter of Dr. and Mrs. Howard Martin Sawyer of North Andover, Mass., July 1. They will live in Baltimore, Maryland.

The Southern Medical Association

Is to hold its annual meeting in St. Louis, November 13-16, under the presidency of Dr. Hamilton W. McKay of Charlotte, North Carolina. Several organizations will meet conjointly with the S.M.A. Scientific and technical exhibits will add to the interest of the meeting. The Kiel Municipal Auditorium will be headquarters for meetings and exhibits.

There are a number of good hotels in walking distance of the Auditorium, but it is suggested that accommodations should be secured by addressing the Housing Bureau, Southern Medical Association, 911 Locust Street, Room 406, St. Louis 1, Mo.

The Pennsylvania Academy of Ophthalmology and Otolaryngology

Held its annual meeting May 12, 13, 14, at the Bedford Springs Hotel, Bedford, Pennsylvania.

In addition to the formal presentation of papers, two Round Table Discussions were held.

The newly elected officers are: President, Dr. Jay G. Linn, Pittsburgh; President-Elect, Dr. Matthew S. Ersner, Philadelphia; Secretary, Dr. Daniel S. DeStio, Pittsburgh; and Treasurer, Dr. Bruce A. Grove, York.

A Medico-Military Symposium

For officers of the Fourth Naval District will be held at the U.S. Naval Hospital, Philadelphia, from October 23 to 28. Speeches and panel discussions are scheduled in aviation medicine, national defense in case of disaster or attack, national preparedness, psychiatry, submarine medicine, surgery, and orthopedics. This is for the purpose of keeping military Reserve Medical Officers of the Armed Forces posted on the latest developments in the field of medical science.

Officers are urged to make reservations well in advance since no government housing facilities will be available. All members of the medical profession are invited to attend.

American Medical Writers' Association

Will hold its annual meeting at the Elks Club, Springfield, Ill., Wednesday, September 27, during the 15th annual meeting of the Mississippi Valley Medical Society, September 27-29. In the afternoon there will be papers by Frank G. Dickinson, Ph.D., Director of the Bureau of Medical Economic Research, American Medical Association and Theodore R. Van Dellen, M.D., Health Editor, Chicago Tribune, with appropriate discussions. In the evening Walter C. Alvarez, M.D., Professor of Medicine, Mayo Foundation, Rochester, Minn., and the Editor of the new publication, *General Practice,* will take over to be followed by a stag entertainment conducted by the Sangamon County Medical Society.

A program may be secured from the Secretary, Harold Swanberg, M.D., 209-224 W.C.U. Building, Quincy, Ill.

Wanted—

Relief doctor for a full month. Must have Virginia license. House, jeep and board furnished with attractive salary. Must be sober. Write William A.

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Cover, M.D., Big Rock, Virginia. (*Adv.*)

For Rent—

Fully equipped office on West Franklin Street in Richmond, to be shared with present occupant at times he is not there. Hours for use can be arranged to suit lessee. Address "Office", care the Virginia Medical Monthly, 1200 East Clay Street, Richmond 19. (*Adv.*)

OBITUARIES

Dr. Charles James Andrews,

Widely known obstetrician and gynecologist of Norfolk, died June 19th at his home there, after a long illness. He was born in Bedford County seventy-four years ago and graduated in medicine from the Medical College of Virginia in 1902. He had practiced in Norfolk for 46 years and it is estimated he had delivered about 8,000 babies in that time. He was a past president of the Norfolk County Medical Society, and was affiliated with a number of other medical organizations in all of which he had been an enthusiastic member. He was for sometime chairman of the Maternal Health Committee of the Medical Society of Virginia. He had also taken an active part in civic affairs and was largely instrumental in getting milk pasteurized in the Norfolk area.

Besides his wife, Dr. Andrews is survived by two sons, both of whom are doctors, and also by a sister.

Dr. Edward P. McGavock,

Of Wytheville, died July the 5th in a Roanoke hospital. He was eighty-one years of age and a graduate in medicine from the University of Virginia in 1893. He lived for many years in Richmond and was formerly professor of Dermatology and Syphilology at the Medical College of Virginia. He retired from practice about ten years ago and went to Wytheville. He was a member of the first Fifty Year Club of the Medical Society of Virginia. A brother is Dr. John F. McGavock of Charlottesville.

Dr. Charles DeVault Prather, Jr.,

Leesburg, died June the 29th, following a heart attack. He was a native of Washington, D. C., and 29 years of age. He graduated from George Washington University School of Medicine in Washington in 1945, and started practice in Loudoun County in the summer of 1947. He was vice-chairman of the staff of Leesburg Hospital and a member of the Medical Society of Virginia. He is survived by his wife and two small daughters as well as his parents.

Dr. Ernest Hamlin Alderman,

Of Richmond, died suddenly on the street June 27th, as he was leaving the City Hall where he had been a witness in a contested will case. Dr. Alderman was born in Greensboro, N. C., in 1891 and graduated in medicine from the University of Virginia in 1921. After serving on the staff of Eastern State Hospital, Williamsburg, he joined the staff at Westbrook Sanatorium in 1928, with which he had since been connected. He was for sometime a member of the Medical Society of Virginia. His wife and several children survive him.

Dr. Herman H. Hines,

Of Pennington Gap, died July the 5th in a Norton hospital. He was forty-two years of age and a graduate of the Medical College of Virginia in the class of 1935. He practiced for a while in Richmond before entering the army in World War II where he served for four and a half years. He received a severe neck injury about eighteen months ago in an automobile accident from which he had suffered from time to time. His wife, mother and a large family connection survive him.

Mr. J. R. McCauley.

It is with regret that we announce the death of Mr. McCauley, secretary-treasurer of the Medical College of Virginia for many years. He had been a member of the staff of the College for 46 years. His death came as the result of a heart attack while he was at work.